ACTA RADIOLOGICA
EDITA IUSSU SOCIETATUM RADIOLOGICARUM
DANIAE, FENNIAE, NORVEGIAE ET SUECIAE

VOL. 53 MAY 1960 FASC. 5

TONIC MUSCLE SPASMS AND BLOOD PRESSURE CHANGES FOLLOWING THE SUBARACHNOID INJECTION OF CONTRAST MEDIA

An experimental study in dogs with injection of Kontrast U and mixtures of Kontrast U and Xylocaine

by

B. Funkquist and *N. Obel*

Thoraco-lumbar myelography using a water-soluble contrast medium (Kontrast U®, Leo) was one of the measures studied during attempts to develop a more accurate diagnostic method in disc protrusion in the dog.

Because of the irritating properties of the water-soluble contrast media, their use in myelography in human subjects has hitherto been limited to the parts of the subarachnoid space which are accessible to spinal anaesthesia, i. e. the lumbar portion. The customary technique, described by ARNELL—LINDSTRÖM in 1931 and later modified by LINDBLOM, among others, is to inject the contrast medium when the previously induced spinal anaesthesia begins to be effective, generally within ten minutes. Reactions such as shock and pain in the lumbar region and lower extremities have been reported by LINDBLOM 1947, DENSTAD 1949, KNUTSSON 1950, PANTER 1953, GROTE 1955, and KOLSTAD 1959. These complications are believed to depend upon an unequal and — because

Submitted for publication 10 September 1959. From the Department of Surgery, Royal Veterinary College, Stockholm, Sweden.

of the injection method used — uncontrollable distribution of the contrast medium and the anaesthetic agent in the subarachnoid space (LINDBLOM & GUND 1955, KOLSTAD).

Any attempt to adapt this method for the introduction of water-soluble contrast media into the thoracic portion of the subarachnoid space is clearly associated with the risk of the anaesthetic agent spreading to the cranial portions of the subarachnoid space during the injection of the contrast medium and producing undesirable effects.

It occurred to us that the short induction time of Xylocaine® might offer the possibility of a new approach in which, unlike the customary method, the anaesthetic agent could be dissolved in the contrast solution and thus injected simultaneously with it. It was also conceivable that by using such a method it would be possible to find a concentration of Xylocaine which would eliminate the irritating effect of the contrast medium without producing any serious vasomotor disturbances.

A. Tonic spasms

1. Experiments on dogs in deep anaesthesia

Four dogs weighing between 5 and 13 kg in deep Mebumal® and nitrous oxide anaesthesia were placed on their sides on a wooden board with a metal strap running along one of the long sides and to which the recording devices were attached. A hind leg was fastened to the plate by means of 3 mm steel pins, two through the tibia and two through the lower part of the femur. The tendons of the gastrocnemius and the superficial digital flexor of the same leg were exposed, sectioned just above the point of the hock, and the proximal ends fastened with steel wire to the recording apparatus. A 5 ml syringe was attached to the metal strap in line with the leg and its plunger was fastened to the steel wires from the tendons and held in place by two springs placed symmetrically. These springs were adjusted so that the muscles were under a tension of approximately 500 g; if the muscles were shortened by 1 cm. the tension would increase to 600 g. The 5 ml syringe was connected by means of a polythene tubing to a 1 ml syringe and the plunger of the smaller syringe was fitted with a writing point. When the system was filled with water, any reduction in the length of the muscles could be recorded on a kymograph.

Anaesthesia was induced with Mebumal, the dog was intubated, and ventilation was maintained with a conventional anaesthesia apparatus with a semi-closed system (AGA, Sweden) connected to a 'Pulmoma' (Dräger Werke). The gas flow to the apparatus was adjusted to 0.5 l N_2O and 2 l O_2 per minute. Respiratory rates were about 40 per minute and the pressures in the anaesthesia apparatus during inspiration and

xpiration were + 150 mm and − 50 mm H_2O respectively. Anaesthesia as so deep during the experiment that nipping a pad of one of the refeet with a towel clamp did not elicit any response.

A 0.7 mm Pitkin needle was inserted into the subarachnoid space etween the fourth and the fifth lumbar vertebrae. The anterior part of ie body was elevated to an angle of about 30° and when the flow of inal fluid ceased, or was reduced to a constant slow drip, Kontrast U 0 % was injected into one of the four dogs used for this part of the study hile the other dogs received Kontrast U together with 1.00, 0.50, or .25 mg/ml Xylocaine hydrochloride, respectively. The Kontrast U Xylocaine solutions were prepared by mixing a Xylocaine solution of wice the desired final concentration with an equal volume of Kontrast U 0 %. For preparing the mixtures, commercial Xylocaine solutions were sed, and for the lower concentrations commercial solutions diluted to suitable concentration with physiologic saline solution. The volume injected was 0.5 ml/kg bodyweight at an injection rate of about 0.5 ml er second. Films were exposed immediately after injection to make certain that all the injected material was in the subarachnoid space. The volume injected was sufficient to fill the subarachnoid space up to the mid-cervical region.

When observations of the effects of contrast alone or contrast with Xylocaine had been recorded, the dogs were allowed to lie undisturbed at the same level of anaesthesia for the next two hours. It was assumed that by this time the greater part of the injected substances would have been absorbed. The same volume of Kontrast U 20 % without Xylocaine was then injected again to test the vitality of the muscles and the sensitivity of the recording devices. In each instance this injection produced a tonic contraction in the muscles attached to the recording apparatus.

In a fifth dog, Kontrast U 20 % with 1.00 mg/ml Xylocaine hydrochloride was injected subarachnoidally under the same experimental conditions, except for the recording apparatus which was replaced by the electromyograph described below under (*2*).

Results. The subarachnoid injection of Kontrast U 20 % into dogs in deep anaesthesia produced a tonic contraction lasting between 10 and 20 minutes in the muscle attached to the recording apparatus (Fig. 1, Ia). When Xylocaine was added to the contrast medium in rising concentrations (0.25 and 0.50 mg/ml), both the intensity and the duration of the reaction were successively reduced (Fig. 1, IIa and IIIa). With 1.00 mg/ml Xylocaine, no contraction measurable with the apparatus used here could be discerned (Fig. 1, IVa). Electromyographic control during injection of a solution of the last-mentioned concentration verified the results obtained by mechanical recording.

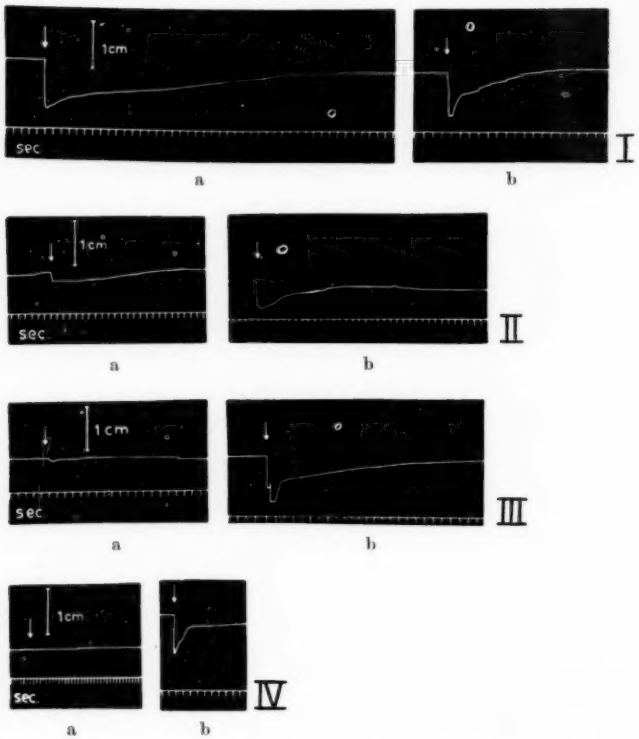


Fig. 1. Contraction of the gastrocnemius and superficial digital flexor in dogs during and after lumbar subarachnoid injection of Kontrast U 20 % (I a). Kontrast U 20 % with 0.25 mg (II a), 0.50 mg (III a), and 1.00 mg (IV a) per ml Xylocaine hydrochloride. The results shown in I b to IV b were obtained by repeating the subarachnoid injection two hours after the first one using Kontrast U 20 % without Xylocaine.

2. Experiments on dogs in light anaesthesia

Four dogs, weighing between 10 and 20 kg, in thiopenton sodium (Intraval Sodium®) and nitrous oxide anaesthesia, were placed with the anterior parts elevated to about 30°. Lumbar puncture with drainage of the spinal fluid was performed in the manner described above. The level of anaesthesia was adjusted so that the animals reacted strongly to pinching a pad with towel clamps by withdrawing the foot. Kontrast U 20 % containing 1.00, 2.00, 3.00, and 4.00 mg/ml Xylocaine hydrochloride was introduced into the subarachnoid space in doses of 0.5 ml/kg body-weight.

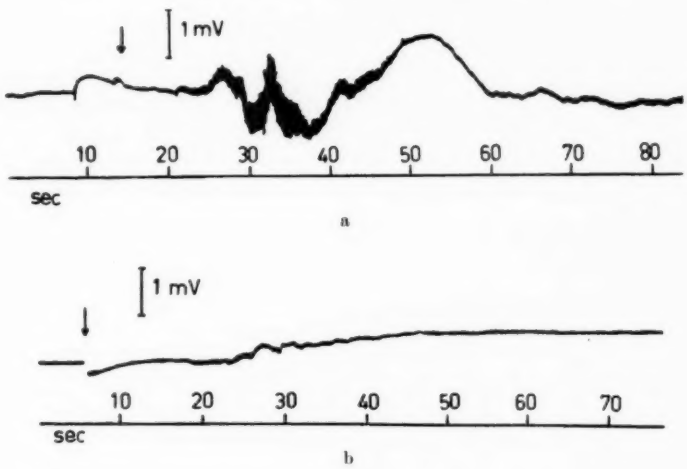


Fig. 2. Action potentials in the gastrocnemius during and after the lumbar subarachnoid injection of Kontrast U with 3.00 mg (a) and 4.00 mg (b) Xylocaine hydrochloride added. Animal in light anaesthesia (retained flexor reflex) during the whole experiment.

During the course of the experiments the action potentials in the gastrocnemius muscles were recorded with a direct-writing myograph ('Mingograph', Elema-Schönander) connected with needle electrodes introduced into the muscle.

Results. The electromyogram for the dogs at such a light level of anaesthesia that mechanical irritation of the pads provoked a strong withdrawal reflex showed a short tonic contraction after the injection of contrast medium with Xylocaine at 1.00, 2.00, and 3.00 mg/ml (duration: 140 sec, 120 sec, and 90 sec, respectively) (Fig. 2a). No muscle response was obtained when Xylocaine was added to a concentration of 4.00 mg/ml (Fig. 2b).

B. Arterial blood pressure and pulse rate changes

Anaesthesia was induced in healthy dogs weighing between 6 and 22 kg with Intraval Sodium and maintained with nitrous oxide as described under 'A'. Succinylcholine iodide (Celocurin Iodide®) intravenously, 0.5 mg/kg bodyweight, produced muscle relaxation and the injection was repeated when spontaneous respiratory movements recurred. Pulmonary

ventilation was maintained throughout the entire experimental perio by means of a 'Pulmomat' (Dräger Werke) as described previously.

The dogs were placed on their right side, the anterior parts wer elevated to about 30°, and the lumbar region was flexed. The subarachnoi space was punctured between the fifth and the sixth or between the fourt and the fifth lumbar vertebrae. When the flow of spinal fluid ceased was reduced to only a few drops per minute at the most, Kontrast 20 % alone or with Xylocaine added (0.31, 0.63, 1.25, 2.50, and 5.0 mg/ml) was injected in a dose of 0.5 ml/kg bodyweight and at the ra of 0.5 ml per second. Films were obtained immediately after the injectio to ensure that all the contrast medium had been deposited in the sul arachnoid space and that it extended forwards to a point between th second and seventh cervical vertebrae (Fig. 9). Only those experiment fifteen in all, in which these requirements were fulfilled will be described

During the entire course of the experiments, the blood pressure i the right femoral artery was continuously recorded by the method o HANSSON & OBEL 1958. The pulse rate was recorded in electrocardiogram taken before and during the injection of the contrast medium, an subsequently at intervals of 1 to 2 minutes during the periods in which the blood pressure varied greatly, and at intervals of 5 to 10 minutes when the blood pressure was steadier.

In order to compare the vasomotor effect of Xylocaine with the combined effect of Xylocaine and Kontrast U, a solution containing 5.00 mg Xylocaine hydrochloride and 75 mg glucose per ml was introduced into the subarachnoid space of three dogs. Three other dogs received Kontrast U 20 % with 5.00 mg/ml Xylocaine hydrochloride. The other experimental conditions were as described above with the exception that the dogs were placed on the abdomen immediately after the roentgen examination, i. e. one or two minutes after injection, to attain uniform distribution of the injected fluids in the subarachnoid space and the most marked vasomotor effect.

The following experiment was carried out to establish the amount of noradrenaline which must be administered per time unit to counteract the vasoconstrictor block induced by the Kontrast U and Xylocaine mixture. Two dogs, anaesthetised and ventilated in the manner described above, were given a continuous intravenous injection of noradrenaline solution (20 μg/ml) at a rate which remained constant throughout a period of some minutes but which was varied from period to period. When an injection rate was attained which gave a moderate rise in blood pressure, the injection was stopped and the dogs were given a subarachnoid injection of 0.5 ml/kg bodyweight of Kontrast U 20 % with 5.00 mg/ml Xylocaine hydrochloride. The correct deposition of the solution was checked by films and then, one or two minutes after the injec

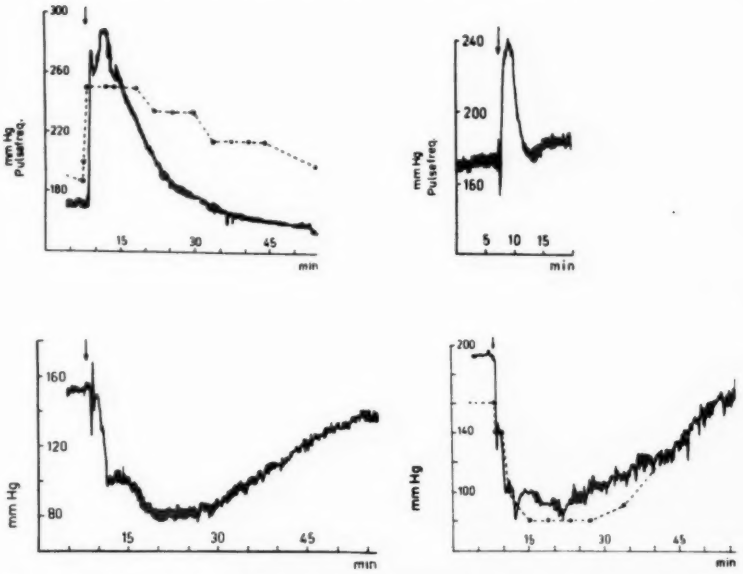


Fig. 3. Blood pressure in the femoral artery during and after the lumbar subarachnoid injection of Kontrast U 20 % and Kontrast U 20 % with 0.31 mg, 1.25 mg, and 5.00 mg per ml Xylocaine hydrochloride. Animal on its side during the whole experiment. The dashed lines indicate the pulse rate.

tion, the animals were placed on the abdomen. When the arterial blood pressure had fallen to about 60 mm Hg, the dogs during periods of some minutes were given noradrenaline intravenously and continuously by means of a motor-driven syringe; the rate of injection was about the same as previously determined.

After the studies were completed, each dog was placed in a special cage with the anterior parts elevated to about 30° for six to twelve hours.

Results. The introduction of Kontrast U 20 % into the subarachnoid space of dogs lying on their side in amounts sufficient completely to fill the lumbar and thoracic portions produced a rise in arterial pressure of more than 100 mm Hg which persisted about twenty minutes (Fig. 3, upper left diagram). The addition of Xylocaine, 0.31 to 0.63 mg/ml, reduced the period of hypertension to about four minutes (Fig. 3, upper right diagram). With a Xylocaine concentration of 1.25 mg/ml, an initial diphasic reaction with a fleeting fall in blood pressure, followed by a rise to or slightly above the original pressure, appeared and was succeeded

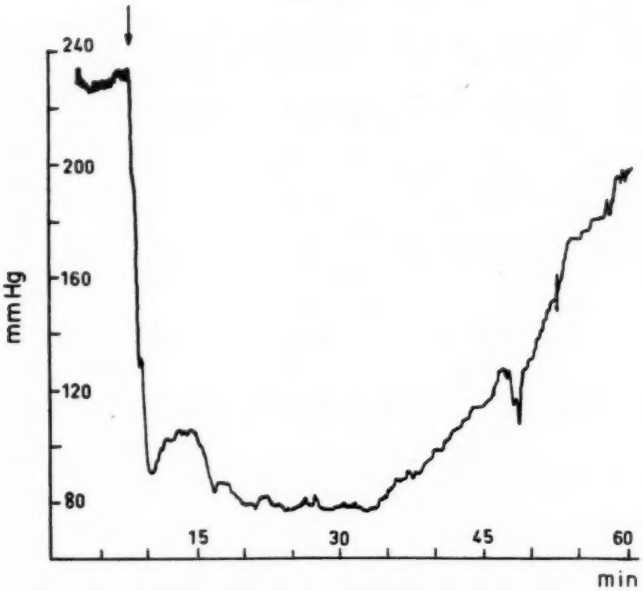


Fig. 4. Blood pressure in the femoral artery after the lumbar subarachnoid injection of 7.5 % glucose solution with 5.00 mg/ml Xylocaine hydrochloride. Animal placed on its abdomen immediately after the injection.

by a slow and moderate depression (Fig. 3, lower left diagram). With 2.50 mg/ml Xylocaine, and even more so with 5.00 mg/ml Xylocaine, there was a rapid and marked reduction in blood pressure which persisted for forty to sixty minutes (Fig. 3, lower right diagram).

The pulse rate varied in accordance with the blood pressure.

In the three animals given a 7.5 % glucose solution containing 5.00 mg/ml Xylocaine hydrochloride into the subarachnoid space and then immediately placed on the abdomen, the blood pressure rapidly fell to about 80 mm Hg; it remained at this level for about twenty-five minutes before commencing a slow return to the original level which was reached about fifty minutes after injection (Fig. 4). Of the three dogs given Kontrast U 20% containing 5.00 mg/ml Xylocaine hydrochloride and then placed in the same position, one developed a rapid fall in blood pressure to about 10 mm Hg ending in cardiac arrest (Fig. 5a). In the other two dogs, the blood pressure decreased to about 45 mm Hg and remained at this level practically unchanged during the succeeding two hours. At this point the artificial respiration was interrupted and cardia-

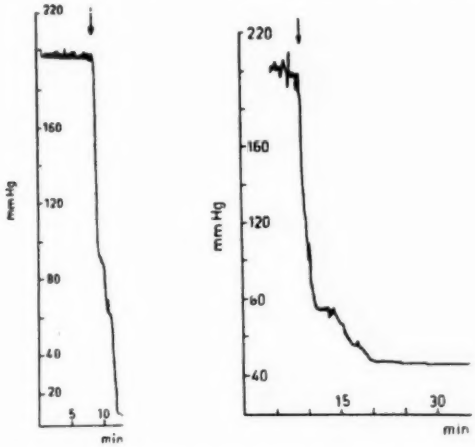


Fig. 5. Blood pressure in the femoral artery of two dogs after lumbar subarachnoid injection of Kontrast U 20 % with 5.00 mg/ml Xylocaine hydrochloride. The dogs were placed on the abdomen immediately after the injection.

arrest occurred without the animals showing any signs of spontaneous respiratory movements (Fig. 5b).

In the two dogs used for studies of the effect of noradrenaline on hypotension induced by the subarachnoid injection of Kontrast U and Xylocaine solution it proved possible to reestablish the original blood pressure by compensating the vasoconstrictor block through continuous administration of 1.0 and 2.8 μg/kg noradrenaline per minute respectively (Fig. 6). The blood pressure level could easily be altered by changing the rate of injection. A marked reduction in blood pressure during the periods when noradrenaline was not administered showed that the inherent tonus of the blood vessels was greatly reduced during the course of the experiment.

The results of these experiments on healthy dogs may be summarised by saying that Kontrast U alone produces a great increase in blood pressure and that by adding increasing amounts of Xylocaine to the contrast medium, this rise may be prevented, or even a fall in blood pressure produced. It is remarkable that such a mixture gives a more marked depression of blood pressure than a similar amount of Xylocaine in a 7.5 % glucose solution.

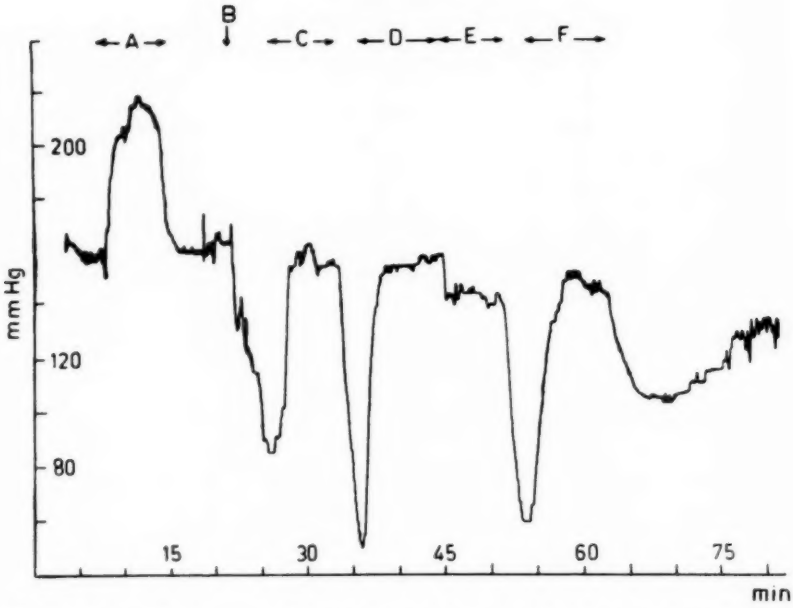


Fig. 6. Effect on blood pressure of the continuous intravenous administration of noradrenaline before and after lumbar subarachnoid injection of Kontrast U 20 % with 5.00 mg/ml Xylocaine hydrochloride. A — 1 μg/kg noradrenaline per min, B — Subarachnoid injection (see above), C — 1 μg/kg noradrenaline per min, D — 1 μg/kg noradrenaline per min, E — 0.6 μg/kg noradrenaline per min, F — 0.3 μg/kg noradrenaline per min.

C. Arterial blood pressure and pulse rate changes during and after myelography on dogs with thoracic or lumbar disc protrusions

Myelography with Kontrast U 20 % to which Xylocaine hydrochloride had been added (1.25, 2.50, or 5.00 mg/ml) was performed on fifty-three dogs (predominantly dachshunds, mean age 5 years, range 2 to 10 years, and weighing between 7 and 10 kg) with clinical signs of spinal cord compression in the lumbar or posterior thoracic region ranging from slight paresis to (in 18 dogs) complete paraplegia. The method largely resembled that described for the experimental dogs although there were some modifications. Much less contrast medium was injected, about 0.30 ml and in a few instances 0.20 ml/kg bodyweight, the position of the body was either horizontal or elevated to 10° or 30°, and the anterior limit of the contrast medium was established roentgenologically in only about a third of the dogs. This limit varied between the second and seventh cervical vertebrae; in one dog it lay above the second cervical vertebra.

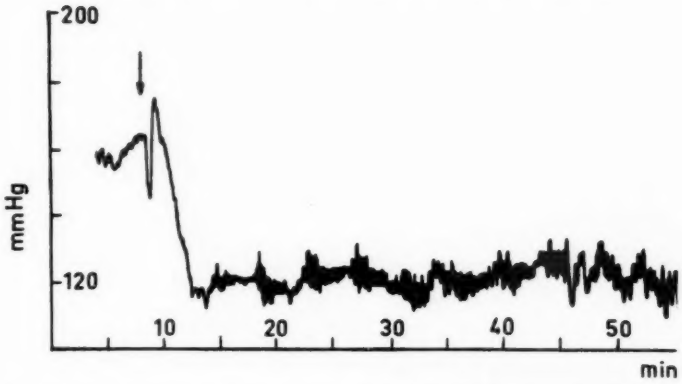


Fig. 7. Blood pressure in femoral artery during diagnostic subarachnoid myelography with Kontrast U 20 % containing 2.50 mg/ml Xylocaine hydrochloride in a dog with clinical signs of disc protrusion. Animal on its side.

Fenestration by the technique of LINDBLOM and OLSSON 1951, was carried out in thirty-four of the dogs. This procedure necessitated the animals being placed on the abdomen at varying intervals after introduction of the contrast medium. If the blood pressure fell to values which could be considered undesirable, if maintained for any length of time (less than 70 mm Hg), noradrenaline solution (20 μg/ml) was slowly given intravenously in repeated small doses as required by the changes in blood pressure. Between 0.01 and 0.08 ml/kg bodyweight per minute for five to twenty minutes were sufficient to prevent dangerous falls in blood pressure.

After myelography, each dog was kept in a special cage with the anterior parts elevated to about 30° for six to twelve hours.

Results. The effect of the Kontrast U and Xylocaine mixture on the blood pressure of dogs with disc protrusions differed in some respects from the results for healthy dogs (Fig. 7). In most of the animals which received contrast medium containing 1.25 mg/ml Xylocaine there was a marked initial rise in blood pressure after injection. A rise also occurred in three of the eight dogs which received 2.50 mg/ml Xylocaine. In the dogs which were given 5.00 mg/ml Xylocaine, the drop in blood pressure was not preceded by a rise. Blood pressure reduction of a magnitude to warrant continuous noradrenaline injection occurred in one of nine dogs given 1.25 mg/ml Xylocaine, in three of eight dogs given 2.50 mg/ml, and in eight of thirty-six dogs which received 5.00 mg/ml.

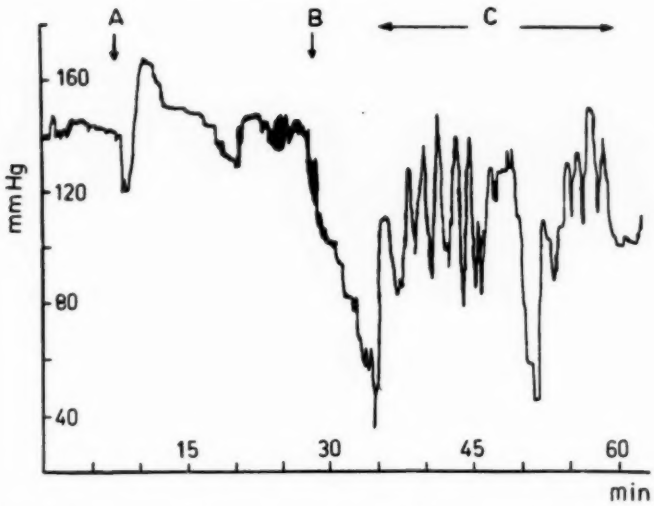


Fig. 8. Blood pressure in femoral artery during and after diagnostic subarachnoid myelography with 3 ml Kontrast U 20 % containing 5.00 mg/ml Xylocaine hydrochloride in a dog (9 kg) with clinical signs of disc protrusion. After 20 minutes the dog was placed on its abdomen for surgery. A — Subarachnoid injection of contrast medium in the lumbar region, B — Animal placed on its abdomen, C — Repeated injections of noradrenaline. Total dose 400 μg.

The pulse rate varied with the blood pressure as described in the experiment dogs.

Placing dogs on the abdomen during the first 40 minutes after the subarachnoid injection increased the chances of obtaining a fall in blood pressure (Fig. 8). Thirteen of the thirty-six dogs which received contrast medium with 5.00 mg/ml Xylocaine were placed on the abdomen for operation within forty minutes. Noradrenaline had to be given to five of these thirteen dogs for various periods in order to maintain satisfactory vascular tonus. In the eight dogs which were operated upon more than forty minutes after the introduction of contrast medium, the blood pressure dropped only by about 10 mm Hg or less after the dogs were placed on the abdomen. Five of the eight dogs which received 2.50 mg/ml Xylocaine contrast medium and seven of the nine given 1.25 mg/ml Xylocaine were placed upon the abdomen within forty minutes without developing any significant drops in blood pressure.

None of the fifty-three dogs upon which myelography was performed because of an existing disc protrusion died during the course of the procedure. Of the nineteen dogs upon which myelography alone was

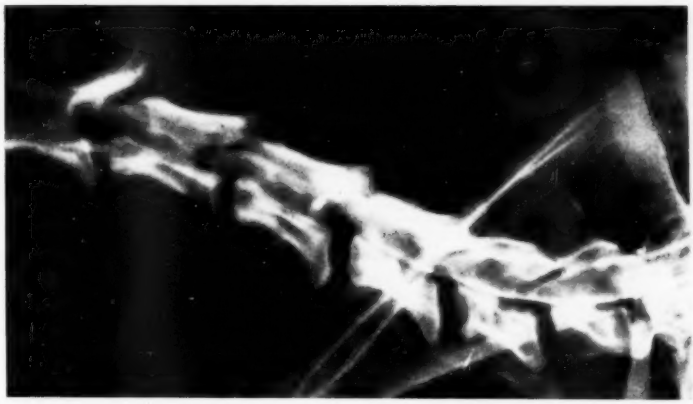


Fig. 9. Roentgenogram of the cervical region of a dog (16 kg) after the lumbar subarachnoid injection of 8 ml Kontrast U 20 % with 5.00 mg/ml Xylocaine hydrochloride (cf. fig. 3.)

carried out, one died within twenty-four hours (purulent bronchopneumonia). Three of the thirty-four dogs in which fenestration was performed directly after myelography died during the post-operative period. Two died within twenty-four hours (shock and myocardial degeneration respectively) and one after two days (no significant lesions other than disc protrusion). The myelography of the last-mentioned dogs did not diverge principally from the other material as regards the circulatory reaction or the distribution of the contrast medium. Neither the circulatory reactions nor the distribution of the contrast medium in these dogs differed from those obtained for the animals which survived.

Discussion

The suggestion upon which our work was based, namely that in place of the technique currently used for lumbar myelography in human subjects it might be possible to utilize a water-soluble contrast medium (Kontrast U) for thoraco-lumbar myelography in dogs by introducing — without any preceding spinal anaesthesia — a contrast solution containing Xylocaine, has proved in many respects to be practicable. The results of the experiments on healthy dogs suggests two possible approaches: (1) Xylocaine may be added to the contrast solution in a concentration of up to about 4 mg per ml to suppress the irritating effects of the contrast medium; (2) The animal may be kept in a state of complete muscle relaxation by means of a short-acting relaxing agent such as

succinylcholine. Then only the vasomotor effect has to be considered when selecting a suitable concentration of Xylocaine.

The favourable experiences of muscle-relaxing agents gained during recent years led to the second approach being chosen for our studies of myelography with Kontrast U in dogs with disc protrusion.

When selecting the concentration of Xylocaine it should be appreciated that an initial rise in blood pressure can be expected in most instances when the concentration is low while increasing the Xylocaine concentration increases the chances of a drop in blood pressure of such a magnitude that the administration of pressor agents may be necessary.

It was demonstrated that a normal and fairly constant blood pressure could be maintained during myelography by the continuous administration of noradrenaline even under conditions which in controls regularly produced a fall in blood pressure of threatening proportions.

The question of whether a low Xylocaine concentration with an initial rise in blood pressure, or a higher concentration with the concomitant risk of hypotension and need for administration of a vasoconstrictor, is safer and therefore preferable cannot be decided without a more extensive investigation.

The fall in blood pressure which can occur when an animal is changed from lateral to ventral recumbency may depend upon the spinal nerves on the upper side being suddenly exposed to the contrast-Xylocaine mixture to a greater degree with the change in position.

It was observed that the hypotensive effect of a subarachnoid Xylocaine injection was augmented by the addition of Kontrast U to the solution. A similar effect in human subjects has been reported by MIFKA 1955, who found that motor activity in the lower extremities which remained after spinal anaesthesia was abolished by the subsequent injection of contrast medium. LINDBLOM (personal communication) has also encountered the same phenomenon and has suggested as an explanation that the mixture of Xylocaine and spinal fluid is displaced upwards by the heavier contrast medium. In our experiments, however, the Xylocaine-glucose solution probably reached the same level in the subarachnoid space as the Xylocaine-contrast solution without producing the same fall in blood pressure. LINDBLOM's suggestion does not appear therefore to offer a satisfactory explanation. For the present we have not gone into the cause of the augmentation of the blood pressure effect.

The risks of filling most or all of the thoraco-lumbar subarachnoid space with Xylocaine and contrast medium mixture appear, *quo ad vitam*, to be surprisingly small especially when one considers that the animals with disc protrusion were generally middle-aged or old and were often completely paraplegic and, furthermore, that the experimental procedure involved anaesthesia for long periods, generally several hours.

Another aspect under consideration is the possible occurrence of tissue damage in the spinal cord and the nerve roots caused by the injection of the large amounts of contrast medium into the subarachnoid space necessary for thoraco-lumbar myelography. The results of these studies will be published separately.

Acknowledgements

This investigation was aided by a grant from AB Leo, Hälsingborg, and from Anslaget för främjande av medicinsk forskning vid Veterinärhögskolan, Stockholm.

SUMMARY

It has been demonstrated in dogs that under light anaesthesia and succinylcholine relaxation, myelography of the thoracic part of the spinal cord may be carried out with a mixture of a water-soluble contrast medium (Kontrast U) and Xylocaine provided that the blood pressure is continuously checked and, if necessary, corrected during the procedure.

ZUSAMMENFASSUNG

Es wurde an Hunden demonstriert, dass während leichter Anästhesie und Succinylcholinerschlaffung Myelographie des thorakalen Rückenmarks mit einer Mischung von wasserlöslichem Kontrastmittel (Kontrast U) und Xylocain durchgeführt werden kann. Voraussetzung ist, dass der Blutdruck fortwährend kontrolliert und, wenn nötig, während der Ausführung der Untersuchung korrigiert wird.

RÉSUMÉ

Les auteurs ont montré sur des chiens que, sous anesthésie légère et relaxation par la succinylcholine, la myélographie de la portion dorsale de la moelle épinière peut être exécutée avec un mélange d'un moyen de contraste hydrosoluble (Kontrast U) et de Xylocaïne, à condition que la pression artérielle soit constamment contrôlée et, si nécessaire, corrigée pendant l'examen.

REFERENCES

ARNELL, S.: Myelography with water-soluble contrast. Acta radiol. (1948) Suppl. No. 75.
— and LINDSTRÖM, F.: Myelography with Skiodan (Abrodil). Acta radiol. 12 (1931), 287.
HENSTAD, T.: The resorption of Abrodil in myelography. Acta radiol. 32 (1949), 428.
GROTE, W.: Die Myelographie unter besonderer Berücksichtigung der Kontrastdarstellung des lumbalen Spinalraumes. Ärztl. Wschr. 10 (1955), 891.
LUND, A.: Ueber eine Komplikation bei der Abrodil-Myelographie und ihre Verhütung. Wien. med. Wschr. 105 (1955), 467.

HANSSON, C.-H. and OBEL, N.: A method for recording blood pressure during operatio . Nord. Vet. Med. 10 (1958), 457.
KNUTSSON, F.: Lumbar myelography with water-soluble contrast in cases of disc-prolaps . Acta orthop. scand. 20 (1950), 294.
KOLSTAD, P.: Myelografi med vannopplöselig kontrastmiddel. (In Norwegian.) Nor . Med. 61 (1959), 306.
LINDBLOM, K.: Lumbar myelography by Abrodil. Acta radiol. 27 (1946), 1.
— Complications of myelography by Abrodil. Acta radiol. 28 (1947), 69.
MIFKA, P.: Ueber die lumbale Myelographie. Wien. med. Wschr. 105 (1955), 364.
OLSSON, S.-E.: On disc protrusion in dog (Enchondrosis intervertebralis). Acta Orthop . Scand. (1951) Suppl. 8.
PANTER, K.: Ueber Komplikationen und Gefahren bei der Abrodil-Myelographie. Dtsc . med. Wschr. 78 (1953), 957.

ROM THE ROENTGEN DEPARTMENT (DIRECTOR: PROF. ERIK LINDGREN), SERAFIMER-LASARETTET, STOCKHOLM, SWEDEN

THE MEDIAL AND LATERAL CHOROID ARTERIES

An anatomic and roentgenographic study

by

James R. Galloway and *Torgny Greitz*

The posterior choroid arteries, which are central branches of the posterior cerebral artery, have thus far received scant attention in both the anatomical and the radiologic literature. In our material, we found an apparent discrepancy between the angiographic changes of the posterior choroid arteries arising from tumors in the pineal region or thalamus, and the changes expected to occur from the reported normal anatomy. This led us to initiate a systematic investigation of this subject.

Previous anatomical studies. In most anatomical text-books no mention is made of the posterior choroid artery. In 'Nomina Anatomica' (Paris 1955) only the ramus chorioideus of the arteria cerebri posterior is designated. In PERNKOPF's 'Topographische Anatomie' the posterior choroid artery is said to have two branches, a medial arising from the superior cerebellar artery and a lateral branch from the posterior cerebral artery. In the monograph on vertebral angiography by KRAYENBÜHL and YAŞARGIL (1957) a single posterior choroid artery is described emerging from the internal occipital artery, a branch of the posterior cerebral artery. NAMIN (1955) described two different posterior choroid arteries,

Submitted for publication 29 September 1959.

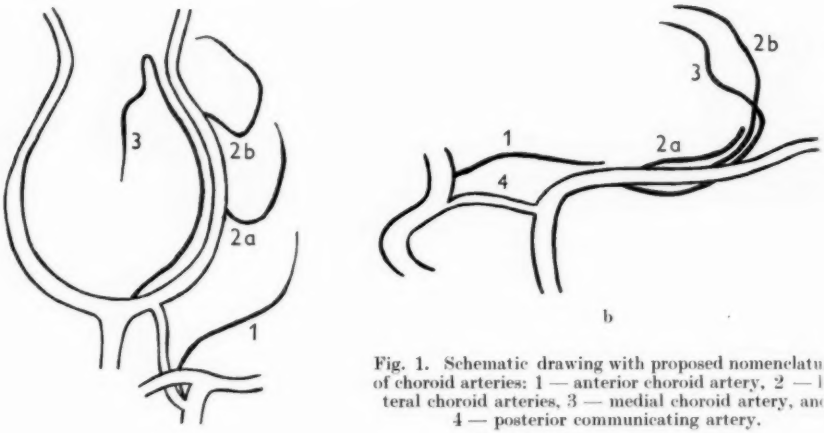


Fig. 1. Schematic drawing with proposed nomenclatu of choroid arteries: 1 — anterior choroid artery, 2 — l teral choroid arteries, 3 — medial choroid artery, an 4 — posterior communicating artery.

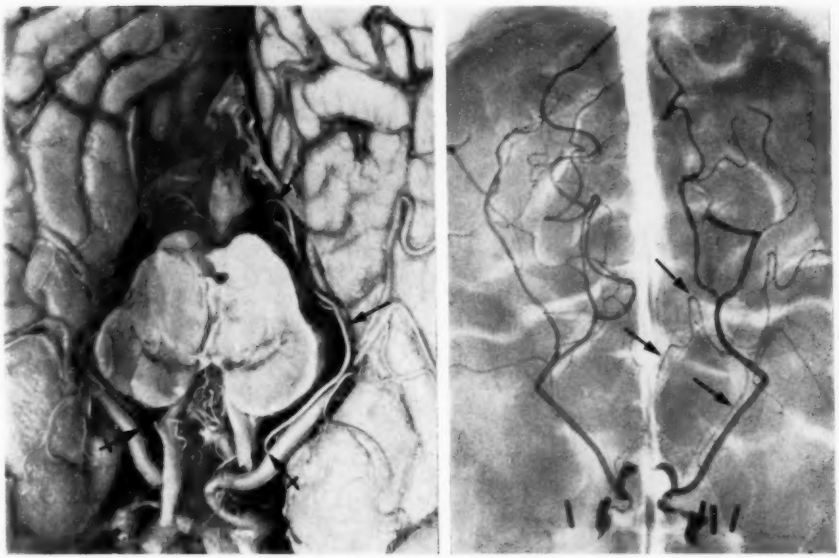
a) half-axial, and b) lateral view.

a medial and a lateral, having a similar course. According to his description, the lateral posterior choroid artery divides into two branches, an external for the superior part of the choroid plexus of the lateral ventricle, and an internal branch for the tela chorioidea. The medial posterior choroid artery should arise posterior to the lateral posterior choroid artery, and lateral to the pineal it should divide into two branches, one for the choroid plexus of the lateral ventricle and one for the tela chorioidea. Accordingly, both the medial as well as the lateral posterior choroid artery should approach the midline. This description has been accepted by LÖFGREN (1958) who added that both the medial and lateral posterior choroid arteries swing out into the choroid fissure, and after approaching the midline and coursing along the roof of the third ventricle, the lateral posterior choroid artery passes through the foramen of Monro. Thus in his description the course of the arteries is similar, and he does not make any clear distinction between changes occurring in the position of the medial posterior choroid artery and those of the lateral posterior choroid artery, as he almost exclusively evaluates changes in the latter vessel.

Present autopsy studies

Material and Method

The anatomy of the posterior choroid arteries has been studied by means of anatomic dissection combined with roentgen examination of the specimens during dissection. The basilar artery was injected at nec-



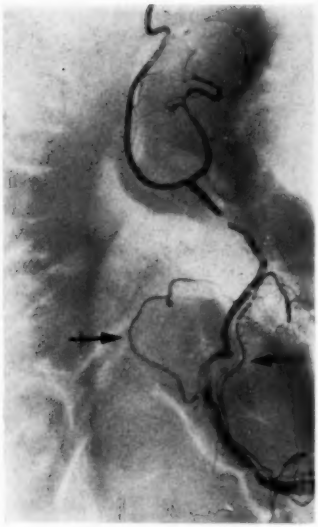
a b

Fig. 2. a) Base of brain with transection of brain stem immediately superior to superior cerebellar arteries. Origin of medial choroid artery (↔) is from posterior cerebral artery, lateral to posterior communicating artery within interpeduncular cistern. Relationship to pineal body should be noted. b) Same specimen, half-axial projection. Medial choroid artery (→).

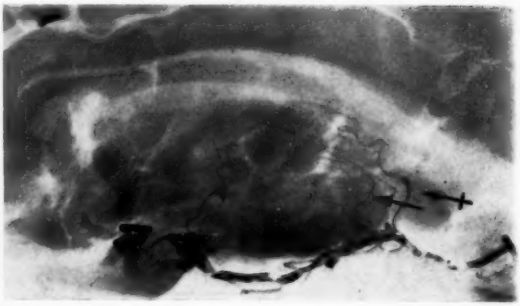
ropsy in 20 cases with a gelatin-barium solution (LINDBOM. JOHANSON) after ligation of the posterior communicating arteries. The brains were suspended in formalin for fixation. As numerous injected cerebellar arteries obscured the posterior cerebral artery and its branches in the roentgen examination, the brain stem was transected immediately superior to the superior cerebellar arteries, and the cerebellum was removed with the superior cerebellar vessels adherent to it, leaving only the posterior cerebral artery and its branches intact within the specimen. The cerebral hemispheres were separated one from the other by a sagittal section through the corpus callosum. On roentgen examination, 26 half-brains had sufficient filling of the posterior cerebral and its central branches for further dissection purposes. The origin and course of the posterior choroid arteries were then determined in each of the selected specimens.

Autopsy findings

It soon became apparent during the autopsy that the current nomenclature was inadequate in that the so-called 'posterior choroid arteries'



a

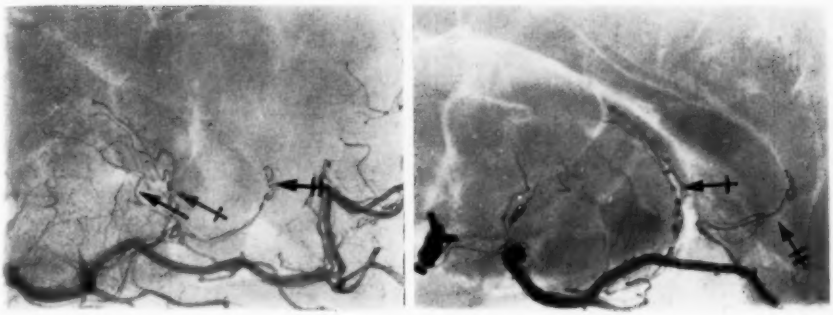


b

Fig. 3. Autopsy material, same specimen as in fig. 5c. a) The basal part of the temporal lobe with its branches from the posterior cerebral artery has been removed and the origin and course of medial (→) and lateral (↔) choroid arteries may be seen. b) Same specimen, lateral projection.

had an entirely separate origin and course. One vessel in its entire course was situated medial to the posterior artery (Fig. 1) and we therefore propose that this vessel be called the 'medial choroid artery'. Lateral to the posterior cerebral artery within the choroid fissure usually lay two arteries for which we suggest the name: the 'lateral choroid arteries' (Fig. 1).

Medial choroid artery. The origin of the medial choroid artery in all 26 half-brains was from the posterior portion of the circle of Willis, or from the posterior cerebral artery within the interpeduncular cistern or crural cistern. The artery runs parallel to the posterior cerebral artery, around and closely adherent to the brain stem, emerging into the quadrigeminal cistern lateral to the pineal body to which it gives off small branches (Fig. 2). Its course, in its situation lateral to the pineal body, as seen from the lateral aspect, roughly resembles a figure of 3 (Figs. 3b, 4a). The inferior limb approaches the middle or posterior pole of the pineal body and then bends forwards toward the anterior pole at the middle of the figure. It then loops posterosuperiorly, bends anterosuperiorly and medially, to course along the roof of the third ventricle in the midline with the internal cerebral vein. As this terminal portion of the artery runs along the roof of the third ventricle, it supplies the choroid plexus



a b

Fig. 4. Autopsy material, same specimen as in fig. 5a. a) Lateral projection showing relationship between medial (→) and lateral (↠) choroid arteries. Posterior pericallosal artery (↠), arising from the posterior cerebral artery, is situated behind them. Anterior to the choroid arteries thalamoperforating arteries are present. b) Same specimen after removal of medial choroid artery. The lateral choroid arteries (↠) are seen in the air-filled choroid fissure behind the thalamus.

of the third ventricle, and may give off small twigs passing under the fornix to the choroid plexus of the lateral ventricle. It may extend almost as far forwards as the foramen of Monro and may form a sharp bend backwards within the tela chorioidea; in none of our specimens did it actually enter the foramen of Monro. In two of the half-brains the medial choroid artery coursing around the brain stem was exceptionally small and there was a supplementary branch arising from the occipital branch of the posterior cerebral artery posterior to the pineal body. In one case it ran directly above the pineal body and in the other lateral to the pineal, in both cases passing forwards to the choroid plexus of the third ventricle, which it supplied in the usual manner.

It will therefore be noted that contrary to the anatomical description utilized by LÖFGREN, the medial choroid artery does not swing out into the choroid fissure across the thalamus but is closely adherent to the brain stem. Neither did it, in our material, course over the pineal body but remained lateral to it; a supplemental branch coursed over the pineal body in one case.

Lateral choroid arteries. We found that instead of one single lateral choroid artery there are usually at least two different arteries (Fig. 5). They arise from the posterior cerebral artery as it passes around the brain stem and immediately enter the choroid fissure. The more anterior lateral choroid artery arises from the posterior cerebral artery usually in the superior part of crural cistern, or in other words, at the superior lateral aspect of the cerebral peduncle. After entering the choroid fissure, it

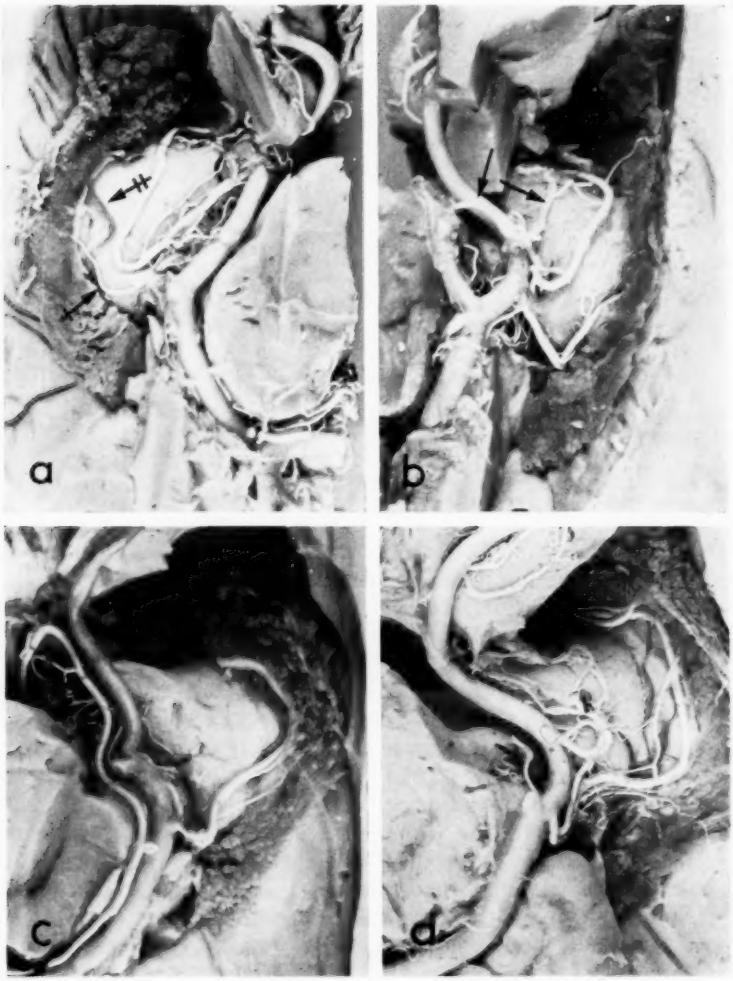


Fig. 5. Autopsy material. Variations in anterior and posterior lateral choroid arteries. The choroid fissure and the temporal horns are opened from below. a) Small anterior lateral choroid artery (↔) and the non-injected anterior choroid artery (↔). Large posterior lateral choroid artery running upon thalamus posterosuperiorly. b) Same brain as in (a) but opposite hemisphere. Usual relationship between anterior and posterior lateral choroid arteries. Auxiliary branch arising from temporal branch of posterior cerebral artery (→). c) One large trunk of lateral choroid artery. The course of the medial choroid artery and its relation to the pineal body should be noted. d) One large anterior and several small posterior lateral choroid arteries.

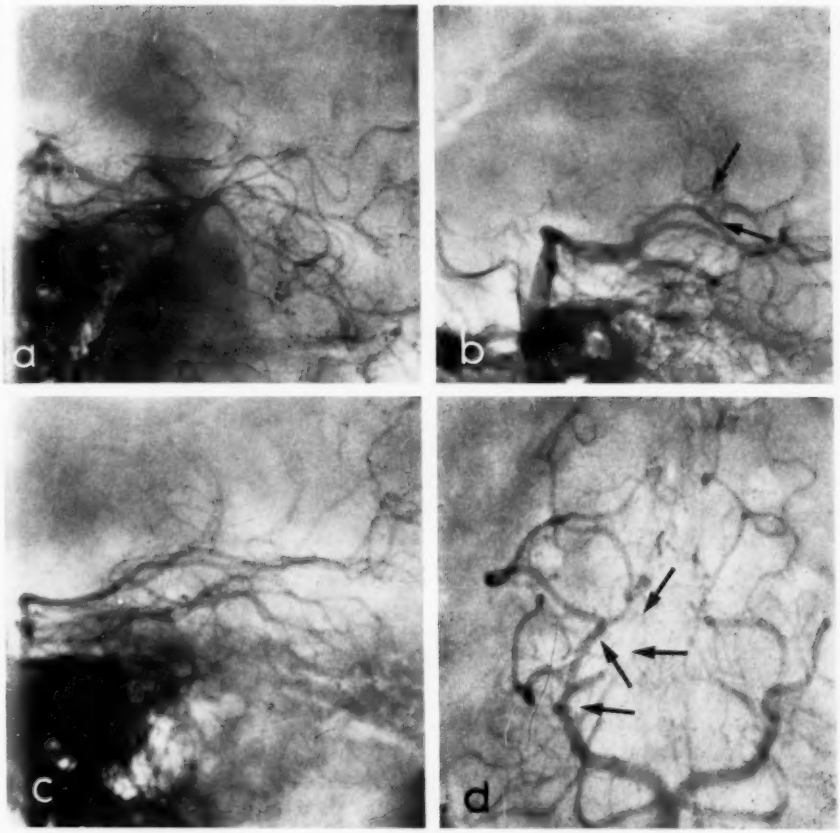


Fig. 6. Vertebral angiography of normal cases. a) The medial choroid artery forms figure of 3. Smooth curve of lateral choroid arteries behind. Small pineal calcification at middle of figure. b) Lower part of figure of 3, formed by medial choroid artery, is partly obscured by an upward bend of posterior cerebral arteries (→). The terminal portion of medial choroid artery forms a sharp bend backwards in tela chorioidea. The posterior pericallosal and the thalamoperforating arteries are well filled. c) Slight difference in the course between the medial choroid arteries. d) Medial choroid artery in frontal projection.

curves forwards and laterally to supply the anterior portion of the plexus of the temporal horn. It may follow the inner aspect of the plexus posteriorly for one or two centimetres. The size of this branch in our specimens seems to depend upon whether the anterior choroid artery, also supplying the plexus, is large or small; when the anterior choroid is large the anterior lateral choroid artery is small and vice versa (Figs. 5a, 5c). The more posterior lateral choroid artery seems to be consistently larger

Fig. 7. Non-filling of posterior cerebral arteries in a case of thrombosis of the left posterior cerebral artery. The entire course of the medial choroid is seen (→).

than the anterior. It emerges from the posterior cerebral artery, usually within the ambient cistern, and enters the choroid fissure. It runs below the thalamus to which it may give off small perforating twigs. In this situation, within the inferior portion of the choroid fissure, it usually gives rise to two branches (Fig. 5a). The most lateral branch, which is usually the larger of the two, curves anterolaterally to the inner aspect of the posterior part of the plexus of the temporal horn, and runs superiorly to supply the region of the trigone and the posterior portion of the plexus of the lateral ventricle. The more medial branch runs superiorly behind the thalamus and ends in the tela chorioidea. We have found that occasionally either the anterior or the posterior lateral choroid artery may be absent, but in any case, the lateral choroid artery which is present is a rather large artery which passes superiorly within the choroid fissure and thus outlines the thalamus in this region (Fig. 5c). Thus, contrary to the anatomical description of NAMIN, and modified by LÖFGREN, the lateral choroid arteries have no relationship whatsoever to the course of the medial choroid artery. They do enter the choroid fissure, and swing around the medial posterior part of the thalamus, but they are vessels which primarily supplement the arterial supply of the anterior choroid artery to the plexus of the temporal horn and the region of the trigone.

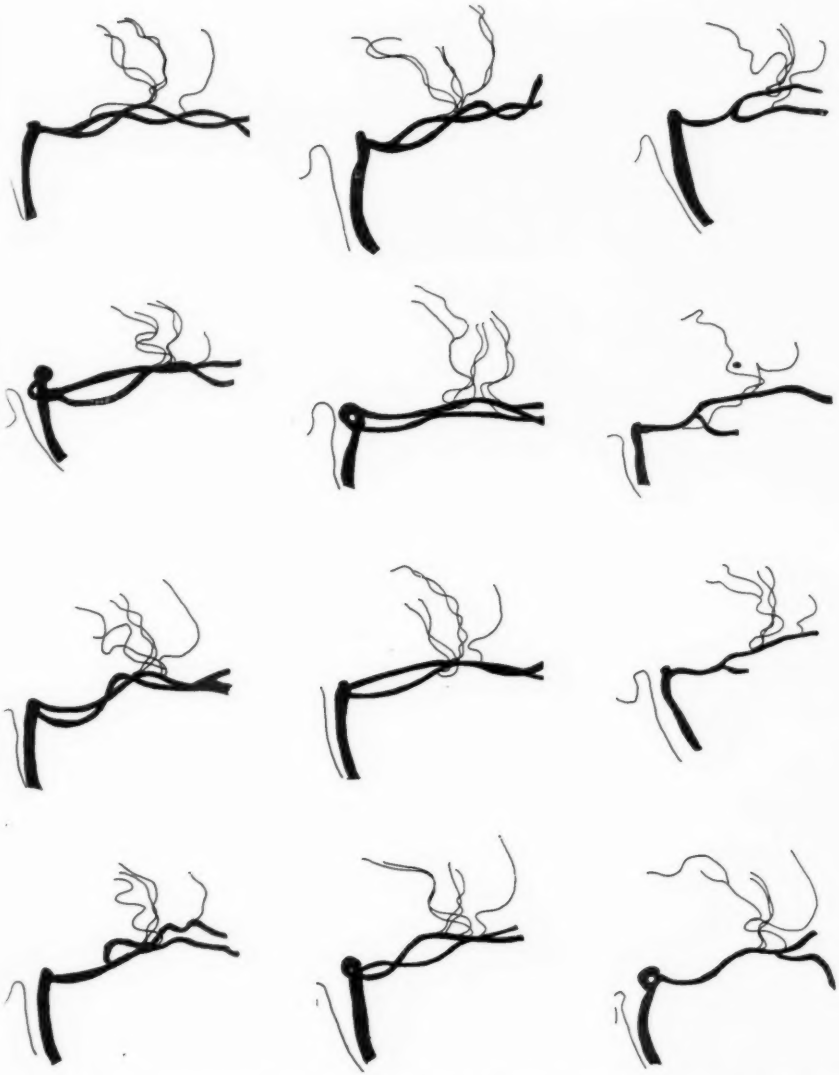
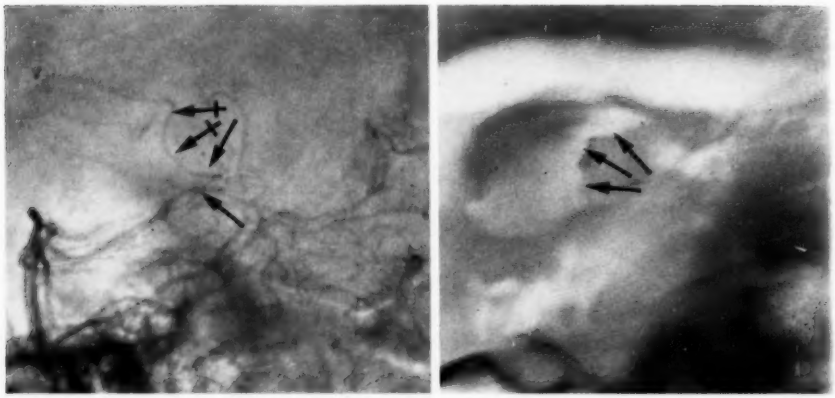
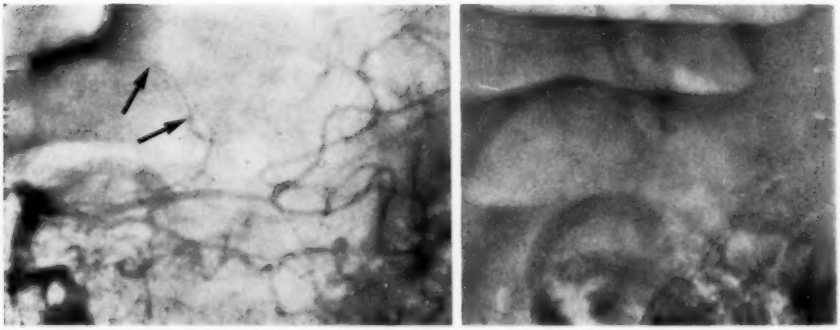


Fig. 8. Sketches of normal variations of medial and lateral choroid arteries. Posterior pericallosal artery is situated behind lateral choroid arteries.



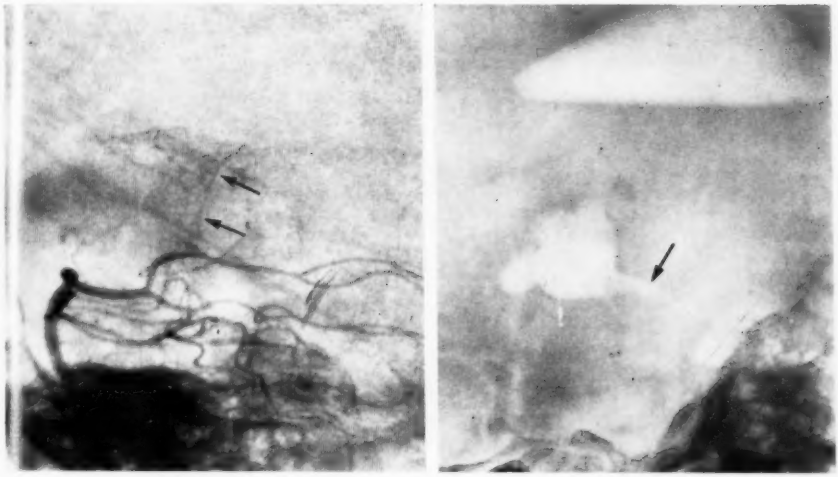
a b

Fig. 9. Small pinealoma. a) Vertebral angiography. Local deformity of medial choroid artery. The usua smooth infero-posteriorly directed curve is now sharp (→). The midportion of the figure of 3 i stretched in a wider curve than normally (↔). b) Same case, encephalography. Relatively smal changes.



a b

Fig. 10. Large tumor in the pineal region. a) Vertebral angiography. The medial choroid arteries (→) are displaced backwards to the level of the choroid fissure. The lateral choroid arteries are relatively unchanged. b) Same case, encephalography.



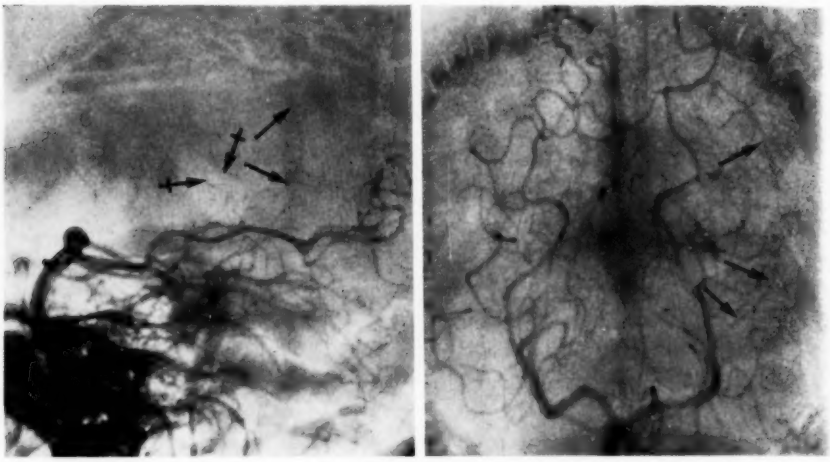
a b

Fig. 11. Cerebellar cyst bulging through the tentorial notch. a) Vertebral angiography. The medial choroid arteries (→) are displaced forwards and stretched. The lateral choroid arteries are unchanged. b) Same case, encephalography. Changes similar to those of meningioma from the free edge of the tentorium cerebelli near the midline. Straightening of the aqueduct (→).

They do not lie adjacent to the pineal body as does the medial choroid artery, and of course they do not pass through the interventricular foramen to supply the choroid plexus of the upper part of the lateral ventricle.

Normal anatomy studied by vertebral angiography

The central branches of the posterior cerebral artery, including the choroid arteries are rarely identifiable in frontal projections as they are superimposed by cerebellar vessels (Fig. 6d). In adequately exposed films, and with good filling of the vessels, it is possible to identify the arteries in lateral views. The medial and lateral choroid arteries are seen to extend upward in a posteriorly directed convex curve from the posterior cerebral artery. It is actually the posterior lateral choroid artery which is seen running above the medial choroid in the larger smooth curve, as it passes posterosuperiorly upon the thalamus in the choroid fissure (Fig. 6). Thus the position of the choroid fissure and the size of the posterior part of the thalamus can be determined. The more anteriorly situated lateral choroid artery has its main extension horizontolaterally, in the inferior part of the choroid fissure and therefore is superimposed by the main



a b

Fig. 12. Thalamus tumor. Vertebral angiography. The lateral posterior choroid artery (→) of the side of the tumor is displaced in a wide bow upwards, backwards, and laterally. The medial choroid arteries (↦) show no changes.

trunk of the posterior cerebral artery in the lateral projection. This also applies to the anterior portion of the medial choroid artery as it curves around the brain stem. Only in the case of non-filling of the posterior cerebral artery can the medial choroid artery, if arising medial to the posterior communicating artery, be seen in its entire course (Fig. 7). The posterior part of the medial choroid artery, as we have previously stated, has roughly the appearance of a figure of 3 in the lateral projection. The figure may form more or less acute bends, but smooth in its relationship to the lateral aspect of the pineal body (Fig. 8). The lower limb of the figure may be superimposed by the posterior cerebral arteries if they bend upward at the pineal body (Fig. 6b). The shape of the artery may vary somewhat on both sides (Fig. 6c). Pineal calcification usually occurs near to the midpoint of the figure of 3, corresponding to the anterior pole of the body (Fig. 6a).

Arterial displacement in tumors affecting the medial and lateral choroid arteries

This study is intended to complement the paper of LÖFGREN, on the use of vertebral angiography in the diagnosis of tumors in the pineal region, in which he described changes of both arteries and veins. LÖFGREN

easured various distances between the bifurcation of the basilar artery d points along the curvature of the lateral choroid artery, in an attempt diagnose tumors arising in the pineal region (tumors arising in the neal body, quadrigeminal plate, or posterior part of the third ventricle). is obvious from the above-described normal anatomy that these easurements do not reflect the growth of expanding lesions in the pineal gion until there has been extension laterally into the thalamus, with nsequent elevation of the choroid fissure. Neither would any similar easurements of expansion of the curvature of the medial choroid artery, early tumors arising in the pineal body, be valid, as the artery is situated teral to the pineal body. The earliest arterial change would consequently a local deformity of the artery adjacent to the pineal body (Fig. 9). s the tumor enlarges there may be an element of posterior displacement f the medial choroid artery (Fig. 10). In an expanding lesion arising osterior to the pineal body, such as a meningioma from the tentorium, the medial choroid artery is displaced forwards, while the lateral choroid arteries may remain unchanged (Fig. 11). If the tumor arises within, or extends into the thalamus, the lateral choroid artery of the side of the tumor will be stretched and displaced in a bow laterally and posterosuperiorly (Fig. 12).

Acknowledgement

One of the authors (GALLOWAY) undertook this study while on a special traineeship, BT-355, from the National Institute of Neurological Diseases and Blindness, U. S. Public Health Service.

SUMMARY

The anatomy of the medial and lateral choroid arteries is described. Contrary to the current anatomical description there is no relationship whatsoever between the medial posterior choroid artery and the lateral posterior choroid arteries, in that the former is in close relation to the brain stem and the midline structures, and the latter are situated laterally within the choroid fissure. A new nomenclature is therefore suggested. Some of the pathologic angiographic findings in tumors localized to specific regions affecting the arteries are described.

ZUSAMMENFASSUNG

Die Anatomie der medialen und lateralen Arteria chorioidea wird beschrieben. Im Gegensatz zur kursierenden anatomischen Literatur besteht keine Beziehung zwischen der medialen- und den lateralen posterioren Aa. chorioideae, da die erstere in enger Beziehung zum Hirnstam und den medial gelegenen Strukturen steht, während die letzteren lateral in der Fissura chorioidea gelegen sind. Aus diesem Grunde wird eine neue Nomenklatur empfohlen. Einige von den pathologisch-angiografischen Befunden bei Tumoren, die diese Gefässe affektieren, werden beschrieben.

RÉSUMÉ

Les auteurs décrivent l'anatomie des artères choroïdiennes internes et extern . Contrairement à la description anatomique classique, l'artère choroïdienne postérieu interne et les artères choroïdiennes postérieures externes ne sont aucunement en rappo du fait que la première est en rapport étroit avec le tronc cérébral et les structures de ligne médiane et que les secondes sont situées plus en dehors, dans la fente choroïdien C'est pourquoi les auteurs proposent une novelle nomenclature. Ils décrivent certains aspects angiographiques pathologiques dans des cas de tumeurs des régions correspondan affectant ces artères.

REFERENCES

JOHANSON, CURT: The central veins and deep dural sinuses of the brain. Acta radi l. (1954) Suppl. No. 107.

KRAYENBÜHL, H. und YAŞARGIL, M. G.: Die vaskulären Erkrankungen im Gebiet r Arteria vertebralis und Arteria basialis. Georg Thieme, Stuttgart 1957.

LINDBOM, Å.: Arteriosclerosis and arterial thrombosis in the lower limb. A roentgenologi l study. Acta radiol. (1950) Suppl. No. 80.

LÖFGREN, F. OLOV: Vertebral angiography in the diagnosis of tumors in the pineal regio . Acta radiol. 50 (1958), 108.

NAMIN, PIERRE: L'artériographie vertébrale. G. Doin, Paris 1955.

PERNKOPF, EDUARD: Topographische Anatomie. 4. Band, 1. Hälfte. Urban & Schwarzenberg, Wien 1957.

ROM THE ROENTGENDIAGNOSTIC DEPARTMENT (DIRECTOR: PROF. KNUT LINDBLOM),
KAROLINSKA SJUKHUSET, STOCKHOLM, SWEDEN

ROENTGEN TELEVISION IN SURGERY WITH SPECIAL REFERENCE TO STEREO-TELEVISION

by

K. Lindblom

The use of conventional roentgen fluoroscopy in surgery necessitates working in darkness and the eyes of the examiner have to be adapted. This disadvantage is eliminated by the image intensifier but other drawbacks appear — the surgeon's field of vision is reduced and his hand is out of his visual control when examining the fluoroscopic image; moreover, he often has to be uncomfortably seated. These technical weaknesses are obviated by transmitting the fluoroscopic image to the screen of a television tube.

Stimulated by the experimental work of MORGAN and others, ordinary roentgen television equipment was tested in our department but proved to be unsatisfactory because it involved the use of unduly high roentgen doses. The experiments were repeated in 1954 and 1955, a combination of an image intensifier and a Vidicon television camera being employed, but satisfactory images were obtained only in thin patients. STAUFFER, MORTON, OPPENHEIMER, & BLACKSTONE reported similar results. WALLMAN & WICKBOM found that a Vidicon camera connected to a Philips amplifier was satisfactory for examinations of extremities.

Since the end of 1958 we have had at our disposal an Orthicon camera coupled to an image intensifier, and as the amplification produced by this combination has proved to be satisfactory, a short report of our experiences may be of interest.

The apparatus has so far been mainly used for the localisation and removal of renal calculi during pyelotomy (Figs 1 and 2). Within the last

Submitted for publication 17 July 1959.

Fig. 1. Television image of renal calculus grasped by forceps.

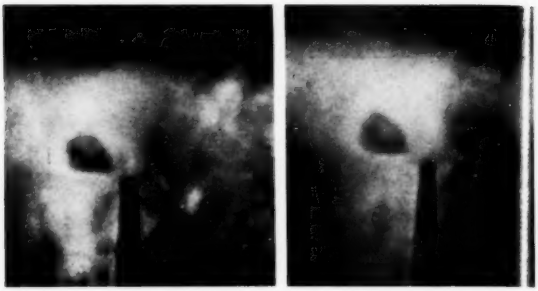


Fig. 2. Stereo-photographs of television image demonstrating position of renal calculus and instrument.

six months it has been used in the control of this operation in 16 cases. It has also been employed for the removal of ureteric calculi, for the reduction and nailing of fractures (Fig. 3), for studying the emptying of the gall-bladder and urinary bladder, and for investigating motility during cholangiography and cholegraphy.

The apparatus consists of a Siemens image intensifier and a Fernseh Orthicon television camera fitted with a conventional receiver, the image being conveyed from the intensifier through lenses and a mirror into the camera. The image intensifier can be rotated about an axis passing through the mirror, which permits of any desired projection.

The method of parallactic displacement is used for localization in the third dimension. The apparatus has recently been modified for stereo-television, a method similar to the well-known one used for stereofluoroscopy being employed. Two roentgen tubes are fitted and are energized alternately at a frequency of 25 c/sec. The two images on the television screen are examined through glasses which have perforated discs which rotate synchronously with each beam cycle. The effect of this is that the two images displayed on the screen of the television tube are seen separately by each eye.

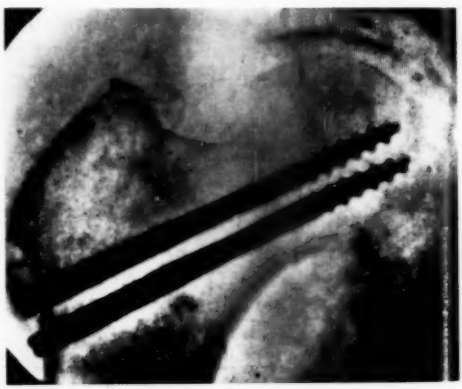


Fig. 3. Photograph of television image during nailing of fracture.

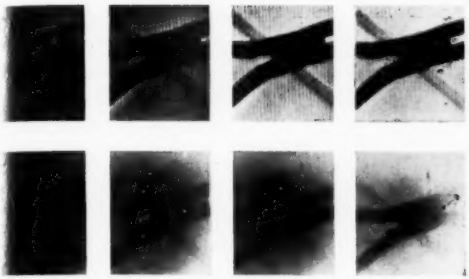


Fig. 4. Photographs of television image: upper series with Orthicon, lower series with Vidicon camera.

Results

The roentgen load required is about the same as that used in conventional fluoroscopy, the maximum load being 65 kV and 2 mA with a focus-image intensifier distance of 50 cm. The television image obtained is bright and of a satisfactory contrast; Fig. 4 illustrates the improved contrast obtained with the Orthicon system as compared with the ordinary Vidicon system.

Excepting in the case of very small renal calculi, say of a diameter of 2 mm or less, the use of roentgen television during nephrolithotomy makes possible the extraction of calculi under visual control. The respiratory movements of the kidney are of major importance in the observation of calculi. Special forceps have been designed for grasping and turning the kidney and have proved to be very useful in assessing paralactic displacement.

Fig. 5. Photograph of positioning for kidney examination. A protective shield is attached to the cone of the tube.

The time required for the reduction and nailing of fractures of the femoral neck has been significantly shortened by the use of roentgen television. The continuous observation during the reduction procedure has been found to eradicate over-reduction.

An important factor to be considered in roentgen fluoroscopy is the possible irradiation danger to the surgeon and his assistant. If a coned down beam is directed towards the image intensifier and if manipulation within the path of the rays is avoided, only secondary radiation will involve radiation hazards. In order to reduce this danger the primary diaphragm of the roentgen tube is fitted with a cone and with a lead which is firmly pressed against the patient's body (Fig. 5). With 65 kV and 2 mA and a moderately obese patient the secondary irradiation dose per minute has been as follows:

	Surgeon (On the side of the image intensifier)	Assistant (On the side of the roentgen tube)
Thorax	< 0.001 r	$= 0.001$ r
Abdomen	< 0.001 r	< 0.001 r
Scrotum	< 0.001 r	< 0.001 r
Hand	< 0.001 r	—

SUMMARY

Roentgen television equipment for the control of surgical procedures and a method of stereo-television are described.

ZUSAMMENFASSUNG

Eine Röntgen-Fernsehanlage zur Kontrolle chirurgischer Eingriffe sowie eine Methode von Stereofernsehen wird beschrieben.

RÉSUMÉ

L'auteur décrit un équipement de roentgen-télévision pour le contrôle des interventions chirurgicales, et une méthode de stéréo-télévision.

REFERENCES

Morgan, R. H.: Application of television electronics to fluoroscopic intensification. Radiology 61 (1953), 111.

Stauffer, H., Morton, J., Oppenheimer. M. J. and coll.: Practical image amplifier tecnics; fluoroscopy, cinefluorography, spotfilm radiography and use with closed circuit television. Radiology 65 (1955), 784.

Wallman, H. and Wickbom, I.: Roentgen-television equipment for use in surgery. Acta radiol. 51 (1959), 297.

FROM THE ROENTGENDIAGNOSTIC DEPARTMENT (DIRECTOR: PROF. SÖLVE WELIN),
MALMÖ ALLMÄNNA SJUKHUS, MALMÖ, SWEDEN

RESIDUAL CONTRAST MEDIUM IN THE BOWEL IN CHOLECYSTOGRAPHY WITH IOPANOIC ACID AND CERTAIN RELATED SUBSTANCES

by

Lars Andrén and *Georg Theander*

Dense granules are often observed in the bowel on cholecystography with iopanoic acid (Telepaque, Bilijodon). Although claimed by the manufacturers of Telepaque to be mainly 'radiopaque material exchanged by the liver and excreted through the bile ducts back into the gut', they are considered by most authors to be the unabsorbed contrast medium. Similar granules are formed in the stomach when tablets of iopanoic acid are decomposed there, whereas in our experience contrast medium expelled from the gallbladder does not produce such granules in the bowel. Though acceptable to some authors as a proof that the patient has taken the medium (BERCOVITZ et coll. 1953, WHITEHOUSE & MARTIN 1953 and 1955) the occurrence of residues is generally regarded as a disadvantage; when abundant, it may confuse the interpretation of the cholecystograms (LOWMAN et coll. 1952) and on the whole may be taken as evidence of incomplete absorption.

An attempt has been made to facilitate the absorption of iopanoic acid by using its sodium salt (Bilijodon-Natrium Leo, in the following referred to as Bi-Na). On exposure of the latter to the hydrochloric acid of the stomach it is converted into an amorphous form of iopanoic acid;

Submitted for publication 1 December 1959.

Table 1

Occurrence of residual contrast medium in bowel at cholecystography with Telepaque (T), Bilijodon (B), and Bilijodon-Natrium (Bi-Na)

	Prep.	Dose in g	Cases	Percentage of cases with residues
Christensen & Sosman 1951	T	3—6	50	Almost 100
Everett & Rigler 1952	T	3	83	80
Lowman et coll. 1952	T	3	100	96
Dunne et coll. 1953	T	2—3	542	Almost 100
Renck 1954	T	3—6	64	53
	B	3	46	43.5
Peterhoff 1956	Bi-Na	2	72	8.5
	Bi-Na	3	128	13
	B	6	140	87
Holmdahl & Lodin 1957	Bi-Na	2	79	38
	Bi-Na	4	121	59
Villaume 1957	Bi-Na	2—2.5	200	3
Zierhut 1957	Bi-Na	2—4	200	4
Own material	Bi-Na	3—6	200	65

this has a larger surface area per unit of weight than the crystalline form present in Telepaque and Bilijodon tablets and is therefore believed to be more rapidly dissolved in the alkaline intestinal juice and, consequently, more readily absorbed. This assumption was supported by comparing the iodine content of the blood following the intake of Bilijodon and Bi-Na (Holmdahl & Lodin 1959). The sodium salt itself is readily soluble and absorbable. Available reports of its clinical use are summarized in Table 1. It appears that though residual contrast medium has been observed in considerably varying frequency by different authors after either preparation, it is as a rule less common after Bi-Na.

In our department, however, no significant decrease was noted in the incidence of residues after 1955, when Telepaque was replaced by Bi-Na for routine cholecystography. A survey of 200 unselected Bi-Na examinations, in which 24 × 30 cm films covering the right hypochondrium were used, revealed residues in 65 %, i. e. a frequency appreciably higher than that observed by most authors. In a search for an explanation of this discrepancy and for a method to obviate the occurrence of residual contrast medium various theoretical possibilities were tested experimentally. The material and results are summarized in Table 2.

The figures given in Table 2 are based on observations made in 30 × 40 cm films covering the abdomen and pelvis. They give more accurate information of the occurrence of residues than can be obtained from the smaller films used in the investigations summarized in Table 1, because

Table 2

Occurrence of residual contrast medium in bowel after 3 g Telepaque or Bilijodon-Natrium (Bi-Na) under different conditions

	Number of cases			Percentage of cases with residues
	With residues	Without residues	Total	
Telepaque	75	6	81	90
Bi-Na	38	5	43	90
Bi-Na with enteric coating	45	9	54	85
Bi-Na with Macrostyrin	33	8	41	80
Bi-Na with EDTA	23	6	30	80
Bi-Na with distilled water	4	8	12	30
Total	219	42	261	

the granules are often irregularly distributed in the bowel. This is reflected by the higher incidence of residual contrast medium found after Bi-Na (Table 2) than in the preliminary survey. In the larger films the residues were demonstrable equally often after Bi-Na and Telepaque in our material.

The solubility of iopanoic acid in water is 0.04 mg/ml at 37°C. The two forms of the substance mentioned in the introduction differ in the rate at which they are dissolved in an alkaline solution. It thus takes more than 20 min for 2 g of the crystalline form to dissolve in 100 ml of a solution of sodium carbonate (20 % excess) at 37°C, whereas 2 g of the amorphous form requires less than one minute. The solubility of Bi-Na in water, on the other hand, is up to 245 mg/ml.

Provided that the residues consist of unabsorbed iopanoic acid, the lower frequency of their occurrence after Bi-Na than after Telepaque and Bilijodon, as stated in the literature, might be explained by the higher dissolution rate of the amorphous form of the acid. A still lower incidence of residues might then be expected after Bi-Na if the breaking down of this salt and the production of the free acid in the stomach could be prevented. An attempt was made to protect the Bi-Na from the action of the gastric juice by administering it in tablet form with an enteric coating calculated to resist the acidity of the gastric juice for at least two hours, but no significant decrease in the incidence of residues was obtained (Table 2). It was, however, observed in some patients that the tablets were retained in the stomach for several hours and ultimately decomposed there. Attempts were therefore made to neutralize the hydrochloric acid in the stomach by the administration of an antacid drug in association with the Bi-Na. The anion-exchanger polyaminostyrene (Macrostyrin NYEGAARD), said to neutralize 55 ml N/10 HCl per gram, was used in

1.8 g doses for this purpose, but again no significant decrease in the incidence of residues was obtained (Table 2).

The failure to reduce the incidence of the residues by these experiments seemed to suggest that in our material they did not consist mainly of iopanoic acid. The demonstration of abundant residues in some cases of achlorhydria examined with Bi-Na gave further support to this suggestion. Attention was therefore focussed on iopanoic acid products of low solubility in water.

The solubility of the aluminium, calcium, iron (ferrous and ferric), and magnesium salts of iopanoic acid in water is low (0.97, 1.07, 0.03, 0.07, and 0.46 mg/ml, respectively, at 37°C). These salts might participate in the formation of contrast residues if the cations required were available in the digestive tract, e. g. supplied by food, beverages, antacid or antianemic drugs, and analgetic or antibiotic agents. As the mains water in Malmö (about 17°dH) precipitates 3.2 g Bi-Na per liter in vitro, the calcium salt of iopanoic acid is in this city presumedly formed whether cholecystography is carried out with the acid or with Bi-Na. In fact, calcium was found to occur in samples of contrast residues obtained from the faeces after examinations with Bi-Na. This might explain the high incidence of residues observed on cholecystography with Bi-Na as well as with Telepaque in our material.

It should be observed in this connexion that substances of low solubility may nevertheless be absorbed from the digestive tract to a fairly large extent. In spite of their low solubility the calcium salt and even the ferric salt of iopanoic acid (given as tablets prepared at our request by AB Leo) were found to outline the gallbladder in some cases. An abundancy of residues was observed after the intake of these substances.

The theory of the significance of the properties of the water in the occurrence of contrast residues received further support when correlation was found between the hardness of the water and the incidence of residues in different districts. Thus, the incidence of residues in Uppsala, reported by HOLMDAHL & LODIN 1957 (Table 1), was little lower than in Malmö but definitely higher than in Lund (PETERHOFF 1956, Table 1). The mains water in Uppsala is 17 to 18°dH and in Lund 14°dH.

Chelating agents such as EDTA (ethylene diamine tetra-acetic acid) are known very effectively to reduce the concentration of metal ions in a solution. As they combine readily with both calcium and magnesium ions, they have been used successfully for softening waters. The administration of 1 g di-sodium EDTA together with the Bi-Na tablets, however, failed to reduce the incidence of residues appreciably (Table 2). In vitro as well, di-sodium EDTA was unable to prevent the formation of the calcium salt of iopanoic acid from Bi-Na in Malmö water.

The simplest way to obviate residual contrast medium consisting of nabsorbed salts would be of course to withhold hard water as well as all ood and drugs containing the metal ions in question. This, however, is ifficult in practice to accomplish in a district supplied with hard water nd it is even more difficult to supervise such a regime. Only twelve atients have been kept under observation in the department and deprived f all food, drugs, and beverages, except distilled water, from the intake of he Bi-Na to the completion of the cholecystographic examination several ours later. Although small, this series of examinations showed a signif-cantly lower incidence of residues than in any of the other methods ried (Table 2).

To sum up, the available evidence seems to suggest that the properties f water are important for the utilization of iopanoic acid in cholecysto-graphy. A similar role may be played by water in the absorption of drugs with a tendency to form salts of low solubility. Treatment with such drugs might then be more or less effective in different regions depending on variations in hardness of the water supply.

Acknowledgements

The dissolution rates and the solubility of iopanoic acid and its salts were determined by the analytical department of AB Leo, Hälsingborg.

SUMMARY

Experiments suggest that when residues of contrast medium appear in the bowel at cholecystography as often with the sodium salt of iopanoic acid as with the acid itself, this is chiefly due to the hardness of the mains water and the resultant formation of salts of low solubility.

ZUSAMMENFASSUNG

Experimentelle Untersuchungen lassen vermuten, dass, wenn bei Cholezystographien Kontrastmittelreste im Dickdarm genau so oft bei Verwendung von dem Natriumsalze der Iopansäure als bei Verwendung der Säure selbst auftreten, so ist dies hauptsächlich durch den hohen Härtegrad des Trinkwassers und die daraus resultierende Bildung von Salzen geringer Löslichkeit bedingt.

RÉSUMÉ

L'expérimentation permet de penser que la présence de résidu de moyen de contraste dans l'intestin au cours de la cholécystographie, aussi bien avec le sel de sodium de l'acide iopanoïque qu'avec cet acide lui-même, est principalement due à la dureté de l'eau de boisson et à la formation de sels peu solubles qui en résulte.

REFERENCES

BERCOVITZ, Z. T., GILLETTE, L. and WHITE, S.: Biliary tract visualization with Telepaque; results in 100 patients. New J. Med. 53 (1953), 2108.

CHRISTENSEN, W. R. and SOSMAN, M. C.: A preliminary report on Telepaque, a new cholecystographic medium. Amer. J. Roentgenol. 66 (1951), 764.

DUNNE, E. F., JENSEN, E. H. and HUGES, C. R.: Telepaque: a new medium for cholecystography. Radiology 60 (1953), 210.

EVERETT, E. F. and RIGLER, L. G.: Cholecystography with Telepaque; Preliminary report. Radiology 58 (1952), 524.

HOLMDAHL, K. H. and LODIN, H.: En jämförelse mellan Bilijodon och Bilijodon-Natrium vid peroral cholecystografi. (In Swedish.) Svenska Läk.Tidn. 54 (1957), 118.

— — Absorption of iopanoic acid and its sodium salt. Acta radiol. 51 (1959), 247.

LOWMAN, R. M., STANLEY, H. W., EVANS, T. S. and MENDILLO, J. C.: A preliminary evaluation of a new cholecystographic medium "Telepaque". Gastroenterology 21 (1952), 254.

PETERHOFF, R.: Cholecystography with the sodium salt of iopanoic acid. Acta radiol. 46 (1956), 719.

RENCK, L.: Experiences with Telepaque, a new cholecystographic medium. Acta radiol. 42 (1954), 336.

WHITEHOUSE, W. M. and MARTIN, O.: A comparative clinical study of Priodax and Telepaque, including 1000 examinations. Radiology 60 (1953), 215.

— — : Clinical and roentgenologic evaluation of routine 2-gram Telepaque dosage in cholecystography. Radiology 65 (1955), 422.

VILLAUME, C.: Cholecystangiografi med Panjopaque; erfaringer med et nyt oralt kontraststof hos 200 ambulante patienter. (In Danish.) Ugeskr. Læg. 119 (1957), 788.

ZIERHUT, E.: Orale trijodierte Gallenkontrastmittel. Chir. Praxis 1957, 407.

FROM THE DEPARTMENT OF PATHOLOGY (DIRECTOR: J. CLEMMESEN) AND DEPARTMENT K (DIRECTOR: JOHS MEYER) OF THE FINSEN INSTITUTE, AND THE RADIUM CENTRE (DIRECTOR: PROF. JENS NIELSEN) AND THE ROENTGEN DEPARTMENT (DIRECTOR: E. DE FINE LICHT) OF THE COUNTY HOSPITAL, COPENHAGEN, DENMARK

ADAMANTINOMA OF THE CAPITATE BONE

by

W. P. Diepeveen, G. H. Hjort and *O. Ch. Pock-Steen*

FISCHER (1913) was the first to describe a tumour of the tibia, histologically similar to the adamantinoma usually encountered in the maxilla. Since then, further cases have been described. FISCHER explained the tibial site on the assumption of an embryonic displacement of a tooth germ. On the other hand, RYRIE (1932) and WILLIS (1948), who have also published cases of tibial admantinoma, suggested traumatic displacement of epithelial tissue which had undergone metaplasia as being the likely cause since there was a striking frequency in the clinical histories of an injury to the limb. These theories were later abandoned and more recent authors (e. g. HICKS 1954 and LEDERER & SINCLAIR 1954) have classified the tumours as mesenchymal growths. CHANGUS, SPEED & STEWART (1957), in a detailed histologic investigation, have tried to adduce that these tumours originate from embryonic angioblasts and have suggested the term malignant angioblastoma. However, 'adamantinoma' or 'tibial adamantinoma', or sometimes 'adamantinoma of the long bones' are now the current designations, although a relationship to the maxillary tumours is no longer accepted.

Tibial adamantinomas are apparently of extremely rare occurrence. CHANGUS et coll. in 1957, in a critical review of almost all the published

Submitted for publication 17 May 1959.

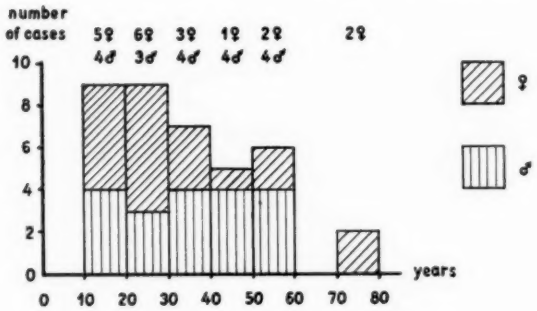
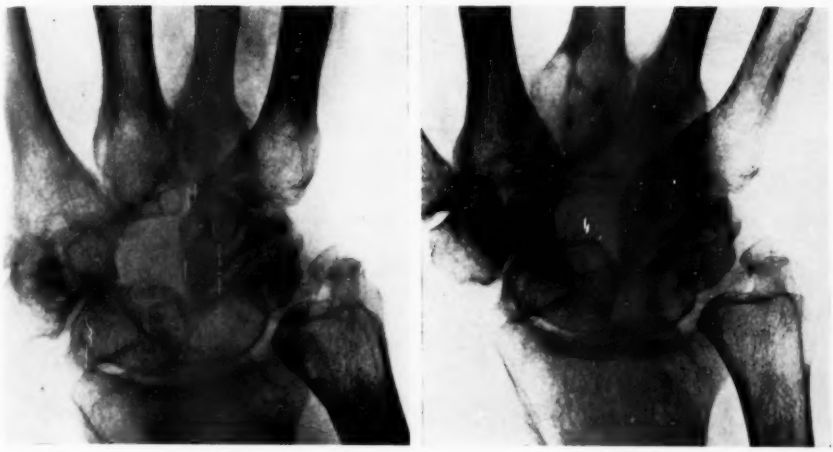


Diagram showing the age distribution in 38 known cases of adamantinoma.

cases, found that there were 25 confirmed cases on record, and they added 6 of their own. In addition to these cases, however, CASINI in 1935, POSSATI in 1948, VANEK in 1951, MARZET in 1954, and MORGAN & MACKENZIE in 1956 have each published a case. Furthermore, HICKS, in 1954, reported a case which he classified as synovial sarcoma of the tibia. Its microscopic appearances were indistinguishable from those of an adamantinoma. In the same year LEDERER & SINCLAIR published a case of 'malignant synovioma simulating adamantinoma of the tibia' in an 11-year-old girl; this case was presumably also one of an adamantinoma. Thus, at least 39 cases appear to be on record.

Clinically, the reported cases have generally shown slow-growing non-tender tumours which had been present for years before symptoms forced the patient to seek advice. Owing to its slow growth, the tumour has sometimes been regarded as benign and treated by local excision which has, however, invariably been followed by recurrence (7, 10). Although the degree of malignancy is low, metastases have been observed in several cases. BAKER, DOCHERTY & COVENTRY, in a follow-up on 18 previously published cases, found metastases in 8 (47 %). The metastases had appeared from 1 to 11 years after the primary growth was diagnosed. MORGAN & MACKENZIE have reported a case of adamantinoma of the right tibia treated by a supracondylar amputation. Twenty-two years later a metastatic deposit was found in a rib (confirmed by biopsy). In LEDERER & SINCLAIR's case a recurrence appeared 3 years after local excision of the tumour. The patient died one year later with evidence of destruction of a rib and pleural effusion.



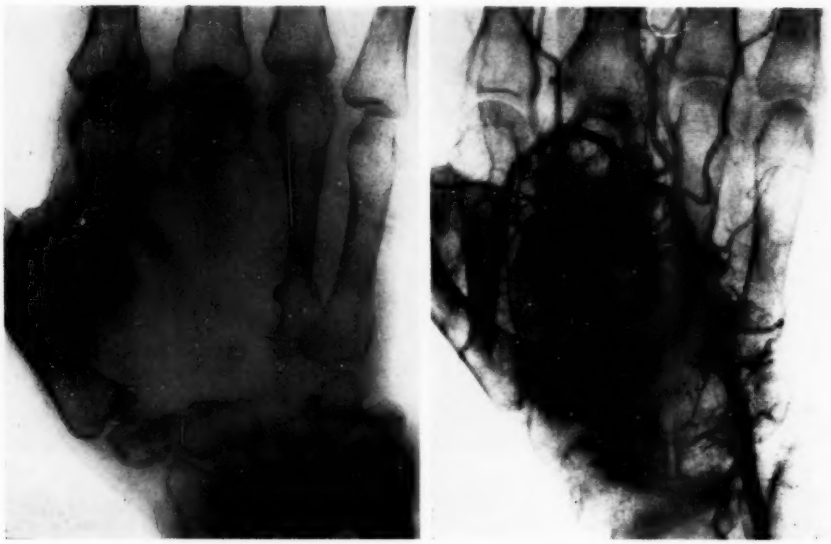
a b

Fig. 1.a) Adamantinoma with total destruction of the capitate bone and incipient invasion of adjacent carpal bones. b) 3 1/2 months later. The destruction at the base of the third metacarpal bone has spread; the bone is enlarged and is the seat of multilocular cystic areas.

Incidence. Adamantinoma appears to occur most commonly in the second or third decade of life. The earliest case on record was observed at the age of 11. There is no predominance of either sex. The age distribution is shown in the Diagram above. The most common site is the tibia which has been affected in 35 cases; a femur was involved in one case and an ulna in another case. Furthermore, in two cases the growth affected a tibia as well as a fibula.

Gross pathology. The adamantinoma is characterized by firm, sometimes brittle, whitish to pink tumour tissue, usually with cystic areas of a gelatinous consistency.

Microscopic appearances. The appearances are predominated by strands, clusters, or whirls of spindle-shaped mesenchymal cells with relatively large, dark-staining nuclei. Another characteristic is the presence of small, round or cleft-shaped cavities lined with a frequently stratified layer of cuboid or columnar cells which have been described as being of epithelial origin. Papilliferous formations of epithelioid cells are occasionally seen in the larger lumina. These cells give a positive alkaline phosphatase reaction like primitive angioblasts, and this was interpreted by CHANGUS et coll. as a sign of a relationship. The substance in the small lumina gives a weakly positive reaction to mucicarmine.



a b

Fig. 2. a) 3 years later. Marked destruction of several carpal and metacarpal bones. The tumour has spread mainly along third metacarpal bone which is completely destroyed proximally and enlarged distally. b) Arteriography via the ulnar artery. Irregular vascularization at the site of tumour, indicating malignancy. No shunts present.

Roentgen findings. The tumour has a multilocular, cyst-like appearance and as it spreads gradually, the bone assumes a spindle-shaped swelling. The tumour has a tendency to grow in the longitudinal direction of the bone, propagating exclusively in bony tissue. It is noteworthy that periosteal reaction is seldom observed although the cortex is eventually entirely destroyed by the tumour. Secondary deposits of calcium do not occur in the tumour and spicules have not been reported.

Case report

A woman, aged 72 years, had fourteen years previously sustained an injury to the right wrist, which was put in plaster. Two years later weakness of the hand developed, and four years before the examination, increasing swelling.

Roentgen examination showed complete destruction of the capitate bone as well as small cyst-like areas of destruction at the base of the third metacarpal and in the hamate bone (Fig. 1a). Control roentgen examination 3 1/2 months later revealed further destruction at the base of the third metacarpal bone (Fig. 1b) and there was halisteresis of all the bones of the hand (atrophy of disuse?). The patient was not seen again until 3 years

ter when a control roentgen examination disclosed marked destruction of several carpal d metacarpal bones; the third metacarpus was completely destroyed (Fig. 2a). A biopsy ecimen was obtained from the tumour and was interpreted histologically as being from glomangioma (Fig. 3a). A reddish-blue, somewhat tense swelling was present around granulating tumour, 3 × 2 × 1.5 cm in size. There was no enlargement of the regional mph nodes.

Arteriography via the right ulnar artery showed irregular vascularization at the site the tumour, indicating a malignant lesion; no shunts and thus no indication that the mour was a glomangioma (Fig. 2b).

Treatment: Amputation of the forearm.

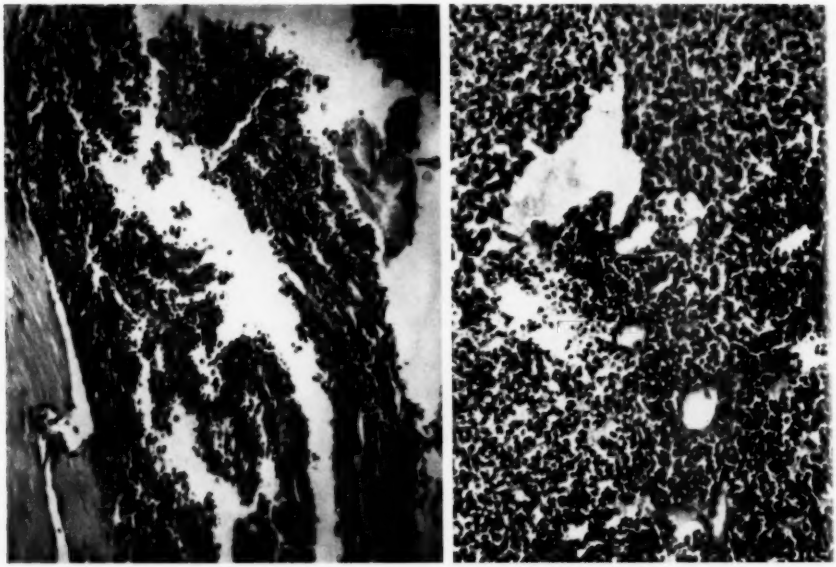
Gross findings: The tumour extended the entire width of the hand from the wrist to he metacarpo-phalangeal joints, destroying the carpal and metacarpal bones, but not involving the muscles or tendons. The latter adhered to the tumour which consisted of reyish-white, fairly soft tissue, solid on section, a cystic cavity as large as a grape (site f biopsy?) lying distally.

Microscopic findings: Invasive tumour cells, forming in places large, solid islets, made p of small anaplastic-like cells with a scanty cytoplasm and predominantly round nuclei f varying chromatin content. Numerous mitotic figures were present. In a few places, here were cleft-shaped or cyst-like cavities with papilliferous formations lined with a ingle layer of cuboid epithelial-like cells with oval or rounded nuclei, these areas being uggestive of a synovial sarcoma. In other regions of the tumour tissue there were more olid islets which in places bore resemblance to the islets encountered in basal-cell carcinoma, and small cystic cavities which suggested an adamantinoma. There was no sign of loose connective-tissue stroma with stellate cells in the cavities, as usually seen in adamantinoma. Special staining with mucicarmine revealed in a few of the cystic cavities a substance taking the mucicarmine stain, and the cytoplasm of the surrounding cuboid cells also contained mucin-positive secretory granules. The tumour is most likely a synovial sarcoma, (Fig. 3b), but an adamantinoma cannot be excluded (Dr. Hjort).

Discussion

The lesion was a slow-growing tumour which had evidently originated from the capitate bone (Fig. 1). Owing to its slow growth it was for a long time considered as being benign. The first histologic report concluded that it was glomangioma, but this diagnosis was ruled out by the subsequent microscopic investigation and the arteriographic findings. Misinterpretations of the motley histologic appearances of adamantinoma have been common (3, 10) and adamantinomas have been mistaken for synovial sarcoma and osteogenic sarcoma.

Hicks in 1954 described two cases of a cyst-like tumour of the tibia, in two women aged 74 and 21; in one the histologic diagnosis was synovial sarcoma and in the other adamantinoma. In the same year Lederer & Sinclair reported a similar cystic tumour in the tibia of a girl, aged 11; in this case the histologic diagnosis was adamantinoma. Both authors emphasized the histologic similarity between synovial sarcoma and adamantinoma. Both show in some areas more solid areas of mesenchymal cells, with relatively large nuclei with an ample chromatin content, and



a b

Fig. 3.a) Biopsy 4 years later. Photomicrograph × 125. b) Amputation specimen 5 years later. Compact areas with anaplastic-like cells and areas showing round or cleft-shaped lumina lined with a single layer of cuboid cells. The appearances are compatible with a synovial sarcoma or an adamantinoma. Photomicrograph × 160.

in other areas epithelial-like cells surrounding cleft-shaped or round lumina. They concluded that there must be a question of the same form of tumour with a marked tendency to differentiation and metaplasia. According to LICHTENSTEIN the substance in the cleft-shaped lumina of a synovial sarcoma gives a positive reaction to mucicarmine, although this also applies to an adamantinoma (3).

Clinically, a tibial adamantinoma can hardly be mistaken for any tumour but a synovial sarcoma. Both are relatively and sometimes even extremely slow-growing tumours (8, 13) which manifest themselves only by increasing, frequently only slightly tender swellings. Synoviomas, however, show a tendency to spread more rapidly after local intervention (8), whereas adamantinomas appear to be far less affected by regional surgery. In several reported cases excision of an adamantinoma has merely resulted in local recurrence. In both types of tumour, however, the course may be fulminant with the early formation of metastases, especially in young subjects (7, 13).

As regards the roentgenologic appearances, there are marked differ-

ıces between a synovial sarcoma and an adamantinoma. In a large series f histologically confirmed synovial sarcomas, SHERMAN & CHU found ıat in every case the site of the tumour was close to a joint, usually a nee joint. A synovial sarcoma always grows on the outside of the bone s a homogeneous, rounded, rather sharply circumscribed soft tissue tuıour. Invasion of the bones may occur, but not until the late stages, and he main part of the tumour is always situated outside the bony structures. ın adamantinoma, on the other hand, is a typical skeletal tumour, ffecting the osseous structures and destroying them from within (3). The ony defect caused by an adamantinoma usually shows a polycyclic lemarcation. In the early stages an adamantinoma is generally interreted roentgenologically as a 'cyst' (3, 6, 7, 9). In the cases published so ar the adamantinoma has always been far from the joints and synovial nembrane. A synovial sarcoma at times contains secondary deposits of alcium (13), which have not been observed in adamantinoma.

It may be impossible to decide from the clinical or histologic findings whether a tumour is a synovial sarcoma or an adamantinoma. This also applied to the tumour in the present case. It was evident, however, from the first roentgen film that the tumour was arising from the capitate bone and not from the articular tissue. The film showed total destruction of the capitate bone with subsequent encroachment upon the adjacent bones, in which, in later films, multilocular, cyst-like areas of destruction had appeared. The authors therefore feel justified in regarding this case as one of an adamantinoma arising from the capitate bone.

SUMMARY

A case of an adamantinoma arising from the capitate bone in a 72-year-old woman is described. Thirty-nine cases of adamantinoma affecting the long bones are on record, but a localization in the carpal bones has not previously been reported. The clinical and histologic features and the roentgenologic differential diagnosis of the tumour are discussed.

ZUSAMMENFASSUNG

Ein Fall von Adamantinom des Os capitatum einer 72-jährigen Frau wird beschrieben. Neununddreissig Fälle von Adamantinom der langen Röhrenknochen sind veröffentlicht, über ein Vorkommen am Os capitatum wurde jedoch bisher noch nicht berichtet. Die klinischen und histologischen Eigenschaften sowie die röntgenologische Differentialdiagnose des Tumors werden diskutiert.

RÉSUMÉ

Description d'un cas d'adamantinome du grand os du carpe chez une femme de 72 ans. Trente-neuf cas d'adamantinome des os longs ont été rapportés, mais on n'avait jamais auparavant rapporté de cas de localisation aux os du carpe. Les auteurs examinent les caractères cliniques et histologiques et le diagnostic différentiel radiologique de cette tumeur.

REFERENCES

1. Baker, P. L., Docherty, M. B. and Coventry, M. B.: Adamantinoma (so-called) o the long bones. J. Bone Jt Surg. 36 A (1954), 704.
2. Casini, A.: Epitelioma malphigiano su antico foculaio osteomielitico della tibia (co detto adamantinoma di Fischer?). Policlinico (Sez. Chir.) 42 (1935), 338.
3. Changus, George W., Speed, J. S. and Stewart, Fred W.: Malignant angioblastom of bone. A reappraisal of adamantinoma of long bone. Cancer 10 (1957), 540.
4. Fischer, B.: Über ein primäres Adamantinom der Tibia. Frankfurt. Z. Path. 1 (1913), 422.
5. Hertz, J.: Adamantinoma of long bones; Report of a case of tibial adamantinoma Acta orthop. scand. 22 (1952), 64.
6. Hicks, J. D.: Synovial sarcoma of the tibia. J. Path. Bact. 67 (1954), 151.
7. Lederer, H. and Sinclair, A. J.: Malignant synovioma simulating 'adamantinom of the tibia'. J. Path. Bact. 67 (1954), 163.
8. Lichtenstein, L.: Tumors of synovial joints, bursae, and tendonsheaths. Cancer 8 (1955), 816.
9. Marzet, M. A.: Un cas d'adamantinome du tibia. Mém. Acad. Chir. 80 (1954), 190.
10. Morgan, A. D. and Mackenzie, D. H.: A metastasising adamantinoma of the tibia J. Bone Jt Surg. 38 B (1956), 892.
11. Possati, L.: A proposito di un caso di adamantinoma della tibia. Bull. Soc. Med. Bologna 120 (1948), 433.
12. Ryrie, B. J.: Adamantinoma of the tibia. Aetiology and pathogenesis. Brit. Med. J. 2 (1932), 1 000.
13. Sherman, Robert S. and Chu, Florence, C. H.: A roentgenographic study of synovioma. Amer. J. Roentgenol. 67 (1952), 80.
14. Vanek, J.: Carcinoma sarcomatodes du tibia. Adamantinome. Rozhl. Chir. 30 (1951) 499.
15. Willis, R. A.: Pathology of tumors. Butterworth, London 1948.

FROM THE ROENTGENDIAGNOSTIC DEPARTMENT (DIRECTOR: PROF. KNUT LINDBLOM),
KAROLINSKA SJUKHUSET, STOCKHOLM, SWEDEN

PARA-AMINOHIPPURIC ACID AS ADJUVANT IN CHOLEGRAPHY

An experimental study in the rabbit

by

Jaan Novek

It sometimes happens in conventional cholegraphy that the contrast density in the biliary tract is poor. Several means of improving the cholegraphic effect have therefore been evolved.

LUDIN & FEINE (1954) increased the amount of bile carrying contrast medium in the bile passages by applying extracorporeal compression over the region of the sphincter of Oddi. BORIS & LÖRINC (1956) secured the same effect by inducing spasm in the sphincter of Oddi with morphine. A method used regularly at this department, and recommended also by CABANIS (1957), is tomography.

EDLING & HELANDER (1958) attempted to increase the contrast density of the biliary tract by injecting a small amount of para-aminohippuric acid (PAH) intravenously immediately before the Biligrafin. They assumed that the renal excretion of Biligrafin would be blocked by the PAH in the same way as with Umbradil. It was thought that the preservation of the blood concentration of Biligrafin brought about by the block would prolong the period during which the contrast medium was excreted by the liver. They recommended the use of 10 ml PAH 20 %.

Submitted for publication 18 November 1959.

If the mean weight of the patient is estimated at 70 kilos, this amount of PAH corresponds to a dose of 0.029 g per kilo bodyweight.

The present writer thought it of interest to study the concentration and excretion of Biligrafin in the bile and urine following the administration of varying amounts of the contrast medium, while at the same time using small amounts of PAH as an adjuvant. These experiments in the rabbit are a continuation of his earlier studies on Biligrafin (NOVEK 1959).

Technique

The experimental conditions and practical arrangements were the same as described in the paper on Biligrafin cited above. The results obtained in that study were used for comparison and are termed controls in the following.

The rabbits were deprived of neither water nor food. The anaesthetic Mebumal was in every instance administered intravenously. The cystic duct was not tied off. Bile was collected via a polythene tube introduced into the common bile duct. The series comprised 11 healthy rabbits.

Each animal received between 0.2 and 0.3 ml PAH 20 % intravenously immediately before the Biligrafin. Since with one exception the animals' weights ranged from 1.70 to 2.05 kilos, this volume amounted to between 0.024 and 0.029 g/kg bodyweight. One of the rabbits weighed 2.95 kilos; this animal was given 0.5 ml PAH, corresponding to a dose of 0.034 g/kg. The Biligrafin was injected in the following doses: 0.12 g/kg bodyweight in 4 animals, 0.32 g/kg in 4 others, and 0.94 g/kg in 3 rabbits.

Samples were taken as in earlier experiments according to a given plan. After introducing the polythene tube, and once the drip rate had become stabilized, the bile flow during a period of 10 minutes was measured. This was termed the control sample. When the PAH and Biligrafin had been injected, the bile was collected during the following standard periods: 0—10 min, 10—20 min, 20—50 min, 50—100 min, and 100—110 min.

Results

The iodine concentration in the bile in the different PAH-series was as follows:

In three of the four animals given 0.12 g/kg bodyweight Biligrafin the maximal iodine concentrations were grouped between 0.49 % and 0.60 %. In the fourth instance, the curve followed a level course with a peak value of 0.28 % (Diagram 1).

In three of the four animals receiving 0.32 g/kg bodyweight of Biligrafin the maximal iodine concentrations lay at or above the 1 % level. In the fourth instance, the concentration curve followed a plateau-like course with a low peak value of 0.58 % (Diagram 2). Since in this last animal the low concentration was associated with a temporarily copious flow of bile, the reduction must be attributed to the admixture of gallbladder bile.

All three animals given 0.94 g/kg bodyweight of Biligrafin had peak values of between 1.25 % and 1.50 % iodine in the common duct bile (Diagram 3).

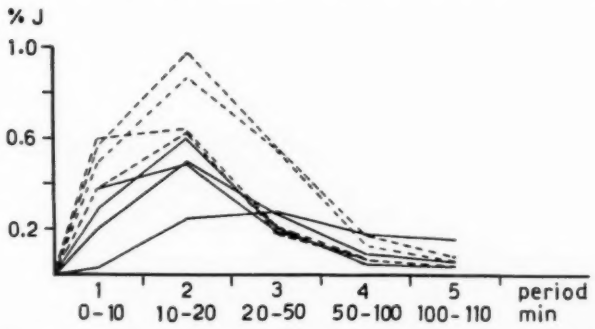


Diagram 1. Iodine concentration in the PAH series (———) and in the controls (- - - -). Biligrafin 0.12 g and PAH 0.02 to 0.03 g per kilo bodyweight.

On comparing the PAH series with the controls, the concentration of iodine in the bile was found not to be increased by the use of PAH. With the exception of the group receiving 0.12 g/kg the iodine concentrations were the same as in the corresponding control series. In the 0.12 g/kg group, on the other hand, the iodine concentration was lower than in the controls.

The configuration of the concentration curves in the PAH series agreed with that in the controls. Depending on the amount of contrast medium

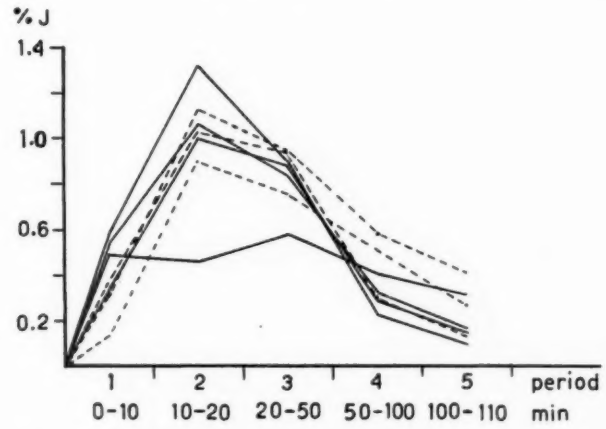


Diagram 2. Iodine concentration in the PAH series (———) and in the controls (- - - -). Biligrafin 0.32 g and PAH 0.02 to 0.03 g per kilo bodyweight.

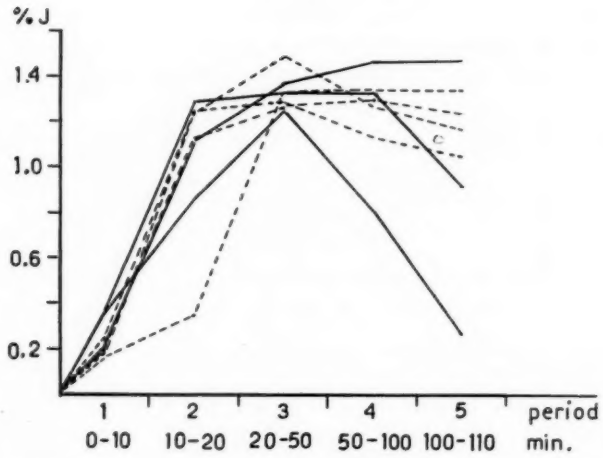


Diagram 3. Iodine concentration in the PAH series (———) and in the controls (- - - -). Biligrafin 0.94 g and PAH 0.02 to 0.03 g per kilo bodyweight.

administered, the maximal concentrations were recorded in the 10—20 and 20—25 min periods or in the 50—100 min period. Once the peak level had been passed, the iodine concentration in the common duct bile fell at an equal rate in the PAH series and in the controls.

Before studying the bile flow, an attempt was made to ascertain whether this was dependent upon the weight of the animal. To that end, the bile volume per kilo bodyweight and per minute was determined. The effects of the operation were minimized by basing these calculations upon the amounts of bile obtained during the 10 min period preceding the injection of PAH and Biligrafin (the control sample). In addition to the 11 experiments in the present series, the results of a further 55 tests in another series were studied; the experimental conditions were identical in all the series. This analysis showed the bile flow to be probably somewhat more copious in light (chiefly young) animals than in heavy rabbits (Diagram 4).

When assessing the effect of the small amount of PAH upon the bile flow following the administration of differing amounts of Biligrafin, the control samples were compared with those collected during the first period following the injection of the two agents (the 0—10 min sample, Diagram 5).

In the group receiving 0.12 g/kg bodyweight of Biligrafin the bile amounts in the 0—10 min sample were lower throughout in the PAH

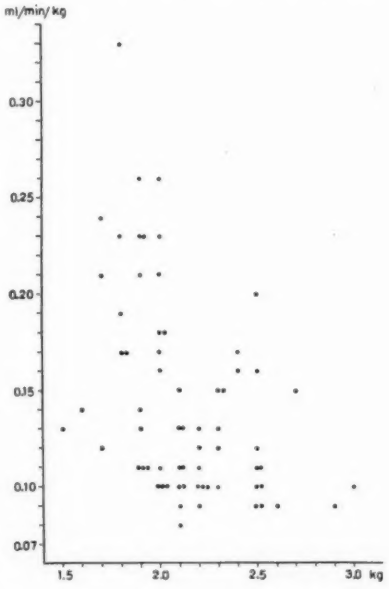


Diagram 4. Relation between bile flow and bodyweight. Calculations based on the values of the control sample.

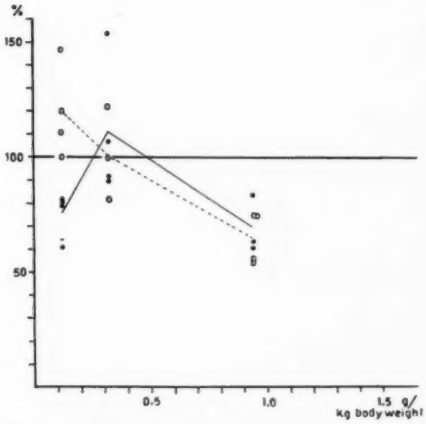


Diagram 5. Bile flow in the PAH series (——— and ●) and in the controls (- - - - and ○). The volume of the control sample taken as 100% and compared with the amount collected during the first period following the injection of Biligrafin.

series than in the control series. In contrast to the raised excretion by the liver of bile in the controls, the PAH animals responded with a decrease in bile flow. This reduction was on the average 24 %.

In the groups receiving 0.32 and 0.94 g/kg the bile flow was with one exception the same in the PAH as in the control series. The dose of 0.32 g/kg induced a rise in the volume of bile in one of the four experiments, while 0.94 g/kg inhibited the flow of bile by 30 % as was expected. In the exception mentioned above, the copious bile flow following the administration of 0.32 g/kg bodyweight of Biligrafin was due largely to emptying of the gallbladder, and in view of the concurrently low concentration not wholly the result of choleresis.

The mean percentage excretion was 37 % in the group receiving 0.12 g/kg, 34 % in that given 0.32 g/kg and 26 % in the animals given 0.94 g/kg bodyweight of Biligrafin. The percentage excretion after the administration of 0.12 g/kg was somewhat lower, and after 0.94 g/kg slightly higher, than in the control series. However, as the series studied were small, the discrepancies are not necessarily significant.

The gallbladder was examined in 4 cases. The amount of contrast medium in the gallbladder ranged from 1 to 3 % of the amount injected. Accordingly, the influence of the gallbladder upon variations in the percentage excretion was very slight. The iodine concentration in the gallbladder ranged from 0.4 to 2.0 %.

The urinary excretion of Biligrafin during the 110 min period varied from 23 to 33 % in the four animals in which this was determined. These values were the same as in the control series.

Discussion and Conclusion

The small PAH dose did not raise the iodine concentration in the common duct bile. In the groups of rabbits receiving 0.32 and 0.94 g/kg bodyweight Biligrafin the concentrations were of the same order as in the control series. In the rabbits given 0.12 g/kg, on the other hand, the iodine concentrations in the PAH series were lower than in the controls. It is as yet not possible to account for this discrepancy.

After passing their peak, the iodine concentrations in the common duct bile in the PAH series and in the controls fell at an equal rate.

The PAH dose given did not increase the bile flow.

The renal excretion of Biligrafin was the same in the PAH series as in the controls. This agrees with the report by Josephson & Kallas (1953) that 5 ml PAH 20 % was too little to have a depressant effect on the renal accumulation when the rabbits were given 8 ml/kg bodyweight Umbradil 35 %.

Acknowledgement

The author wishes to express his sincere thanks to AB Pharmacia, Uppsala, whose financial aid and iodine analyses made the study possible.

SUMMARY

In experimental cholegraphic studies in the rabbit, a dose of 0.02 to 0.03 g/kg bodyweight PAH 20 % given simultaneously with Biligrafin did not raise the iodine concentration of the bile, nor was any decrease in the renal excretion of Biligrafin noted.

ZUSAMMENFASSUNG

Bei experimentellen cholegraphischen Studien am Kaninchen ergab die Verabreichung von 0.02 bis 0.03 g/kg Gewicht PAH 20 %, welches gleichzeitig mit Biligrafin verabreicht worden war, weder eine Erhöhung der Jodkonzentration in der Galle noch eine Verminderung der renalen Biligrafinausscheidung.

RÉSUMÉ

Au cours d'études cholégraphiques expérimentales sur le lapin, une dose de 0.02 à 0.03 g de PAH à 20 % par kg de poids corporel administrée en même temps que la Biligrafin n'a pas augmenté la concentration d'iode dans la bile et n'a pas permis de noter de diminution de l'excrétion rénale de Biligrafin.

REFERENCES

Boris, A. und Lörinc, P.: Vorzuge und Nachteile der mit Morphinwirkung kombinierten Biligrafinuntersuchung. Fortschr. Röntgenstr. 84 (1956), 305.

Cabanis, H. W.: Indikation zur Schichtaufnahme bei der Gallenkontrastmitteldarstellung und ihre Technik. Fortschr. Röntgenstr. 87 (1957), 465.

Edling, N. P. G. and Helander, C. G.: Cholegraphy with depression of the renal excretion of the contrast medium. Acta radiol. 49 (1958), 187.

Josephson, B. and Kallas, J.: Iodine concentration in rabbit kidneys after Diodrast injection. Amer. J. Physiol. 174 (1953), 65.

Ludin, H. und Feine, U.: Ausscheidungs-Cholegraphie mit Kompression. Fortschr. Röntgenstr. 81 (1954), 314.

Novek, J.: Concentration of the contrast medium Biligrafin in the bile and urine in cholegraphy. Acta radiol. 52 (1959), 417.

FROM THE INSTITUTE OF RADIOBIOLOGY (DIRECTOR: LABORATOR A. FORSSBERG), KAROLINSKA INSTITUTET, STOCKHOLM, SWEDEN

INVESTIGATION OF THE CURATIVE EFFECT OF LYCOPENE IN IRRADIATED MICE

by

Arne Forssberg, Gunnar Walinder, Minoru Fujita
and
Gudrun Dreyfus

In a previous publication (4) it was shown that lycopene suspensions, given intraperitoneally before or shortly after irradiation, improved the recovery and survival of roentgen irradiated mice. Some difficulties to reproduce the results were met with, since the beneficial influence of the lycopene treatment was found, inter alia, to be dependent on the amount of the substance given and on the time of its injection relative to the time of irradiation. This was particularly the case when lycopene was given after irradiation; at certain time intervals between the irradiation and the lycopene injection additional damage resulted, as shown by an increase in the death rate of the animals. Still another factor which evidently influences the results is the particle size of the ground lycopene crystals of the suspension.

As we considered that the first stage of the lycopene action might be connected with a resorption of the injected material from the peritoneum, we attempted to control the rate of this process. The question arose as to whether a retardation of the resorption rate in post-irradiation treatment would improve the results. We found that polyphloretin phosphate (PPP), a strong inhibitor of hyaluronidase activity and a substance which has been proved to decrease the permeability of colloidal or particulate

Submitted for publication 9 October, 1959.

matter through the serous membrane (5, 6, 7), somewhat improved the result. This procedure of stimulating the recovery is, however, in our experience difficult to control, evidently due to the complexity of the reactions which are initiated in the body.

Some attempts were also made to inquire into the mechanism of this modification of the radiation damage. It will be shown that the haemopoiesis of the irradiated and treated mice is stimulated to an earlier activity than the mice which were only irradiated, and that concomitantly the spleen and the suprarenals increase considerably in weight.

Material and Methods

Heterozygote white mice, 21 to 27 g in weight, from our own breed, were used; they were of the same sex and approximately of the same weight within each series of experiments. The animals received 24 hours before irradiation, an intraperitoneal injection of 0.5 to 2 mg PPP suspension (molar weight ~ 15 000; product of Leo, Hälsingborg, Sweden). After whole body irradiation with 700 to 750 r (165 kV, filter 0.1 Cu + 1 Al), suspensions of 50 to 100 γ lycopene (Hoffmann-La Roche synthetized compound) were given intraperitoneally at the times stated in the text. The lycopene suspensions were made up in a Tween 80-saline mixture as given in the previous publication. Trials were made with lycopene particle suspensions of varying coarseness, although the long needle-shaped crystals of lycopene makes a precise definition of the size practically impossible; in our experience amorphous lycopene, obtained from petrol ether solutions, and therefore more satisfactory as regards control of particle size, was biologically rather ineffective.

In experiments relevant to studies of the haemopoiesis, radioactive iron, Fe^{59}, with a specific activity of 100 to 150 μC per mg Fe, was given subcutaneously in amounts of about 0.3 μC per animal. The animals were sacrificed 24 hours after the injection and the blood and spleen removed for analysis. The centrifuged blood sediment was washed free from soluble Fe^{59} in slightly hypertonic saline and dried. In one series of experiments haemin crystals were isolated as pure crystals through the usual glacial acetic acid procedure and analysed for activity. The weighed fresh spleens were extracted with 5 % trichloracetic acid and were then further washed in alcohol-ether and dried. Radioactivity was assayed in aliquot amounts of the samples. In some experiments attempts to correlate the early capacity of haemin synthesis of the irradiated animals with the prospects of a 30-day survival were made and slightly higher amounts of Fe^{59}, or 0.5 μC per animal, were given on the 7th day following irradiation. Blood samples of about 0.1 ml were drawn from the tail vein 24 hours later and were dried and counted for activity. A material of some 100 animals furnished indications that mice which survived for 30 days showed generally higher haeminsynthetic activity than those dying earlier. The correlation was, however, not very strong, indicating that other factors are of prime importance in the recovery process. This experimental material will therefore not be considered in detail.

In a few series the rate of formation of new spleen tissue was followed at various times after irradiation by analysis of the incorporation of C^{14}-2-glycine; 0.33 μC per mouse was injected into the peritoneum and the spleens were secured from the sacrificed animals 24 hours after the injection. Soluble C^{14} compounds were extracted twice with 5 % TCA and the remainder was washed in alcohol-ether, dried, and counted for activity. The C^{14} incorporation from labeled glycine is practically equivalent to protein and nucleic acid synthesis in the non-soluble rest.

Results

We had earlier found that the administration of lycopene at certain times, e. g. 4 to 7 hours after irradiation, often produced additive damage as shown by increased death rates. Doses of the order of 25 to 100 γ were mostly beneficial when given within the first hour, although the experiments were difficult to reproduce quantitatively; 100 γ for example occasionally caused additional damage.

In the present experiment it was found that the injection of 1 to 2 mg colloidal PPP 24 hours before irradation, followed by lycopene treatment 30 min after the roentgen dose, increased the survival figures as compared to a series in which the PPP injection had been omitted (Table 1). PPP given alone did not improve the survival.

The average survival in groups of animals given 725 r without additional treatment is in our material about 5 to 10 %. In the present material the increase in the survival after administration of lycopene alone was slightly higher in the 100 γ group and slightly lower in the 50 γ group than previously found (4). From the figures in Table 1 it would seem however that pretreatment with PPP somewhat improves the recovery. The difference between the survival figures in the groups given additional PPP treatment and those given saline is significant at the $P_{0.001}$ level. From further experiments we had indications of a correlation between animal weight and the amount of PPP to be given in order to produce optimal recovery, although it would take much material to establish reliable data; 0.5 mg was, however, clearly suboptimal in the test on 23 g animals given in Table 2, whereas 1 mg gave the best results. The 25 to 27 gram-mice were usually given 2 mg. As stated above, the recovery process is accompanied by a weight increase of the suprarenals. This is clearly indicated in the present series.

In some preliminary trials it was observed that the haemopoiesis was improved in the PPP-lycopene treated animals. In connection with this

Table 1

The effect of pretreatment with PPP (Groups 1 and 2) as compared to series in which the PPP injections had been omitted (Groups 3 and 4)

Group	Number of mice	2 mg PPP (saline) 24 hrs before the roentgen dose	γ lycopene 30 min after irradiation	30 days survival, %
1	53	PPP	100	42
2	55	PPP	50	68
3	55	Saline	100	15
4	54	Saline	50	29

Table 2

Correlation between the survival of 23 g female mice (30 per group) given 725 r followed by 50 γ lycopene, and the amount of PPP injected 24 hours before irradiation. Dry weights of lipid-free suprarenals; average of material from 24-day survivors.

Mg PPP in pretreatment	Roentgen (+) lycopene (l)	24-day survival, %	Suprarenals, mg lipid-free and dried/animal
—	Only l	100	0.48
0	+, l	16.5	0.79
0.5	+, l	20.5	0.98
1.0	+, l	63.5	0.82
2.0	+, l	43	0.78

we also found that the spleens of the treated animals lost initially less in weight and regained in weight more rapidly than did the spleens from the animals which had received only roentgen treatment. The appearance of Fe^{59}-labeled red cells in the peripheral blood of irradiated animals given radioactive iron is an indication of renewed haemopoietic activity of the reticulo-endothelial system. In the present case it was found that the production of new labeled red cells did not occur until 6 to 8 days after irradiation. The main series of experiments was then performed between the 7th and 14th day. A representative series of experiments is summarized in Table 3.

From each of the two groups of mice 4 or 5 animals were injected with Fe^{59} on the 7th, 9th and 14th day after the irradiation. They were sacrificed 24 hours later and analysed. In the control group 'saline + 725 r + saline' the spleen weights are low on the 8th day and the recovery, judged from the weight increase, is very poor in the second post-irradiation week. The formation of new red cells has barely started on the 8th day, as seen from the Fe^{59} activity values, but improves somewhat during the week following. In the PPP-lycopene treated group the picture is more promising. The fairly rapid increase in spleen weight and blood activity points to recovery processes. The Fe^{59} activity of the peripheral red cells on the 15th day in this group was found to be nearly of the same order of magnitude as in the non-irradiated animals.

The specific blood activity increases generally much more rapidly with time than the spleen recovers in weight; this is particularly evident in the control group of Table 3 where the average spleen weights, as against the blood activities, do not increase significantly. This implies that a partial recovery of the haemopoiesis takes place without any parallel net gain in spleen tissue mass. A similar conclusion is arrived at from the fact that the Fe^{59} activity of the spleen is very low at the 8th day

Table 3

Fresh weight and Fe^{59} activity of spleen and the Fe^{59} activity of dried red cells

Group	Analysed on day after irradiation	Spleen weight mg	Average	Counts/min per mg dried spleen	Average	Counts/min per 20 mg dried cells	Average
Saline + 725 r + saline	8	18.6	19.5	10.4	9	1.0	5.5
		14.6		6.8		3.4	
		20.4		5.0		1.6	
		24.4		14.0		16.1	
	10	19.7	28	12.4	37	5.9	35
		29.6		59.2		20.2	
		26.0		5.4		3.1	
		37.3		48.6		65.6	
		26.3		58.0		80.2	
	15	42.8	28	106.2	76	333	108
		19.5		34.4		48.6	
		33.5		141.8		19.8	
		17.7		21.6		30.9	
PPP + 725 r + 50 γ lycopene	8	39.6	29	85.2	67	116	39
		22.1		13.7		9.1	
		26.4		15.9		10.7	
		28.4		153		20.0	
	10	43.9	39	40.4	85	49.6	99
		33.0		50.8		96.1	
		23.9		216		60.4	
		41.1		29		59.8	
		52.1		90.2		230	
	15	26.8	95	60.0	80	426	545
		195.3		50.4		750	
		104.4		98.4		595	
		69.5		85.2		313	
		79.8		104.6		640	

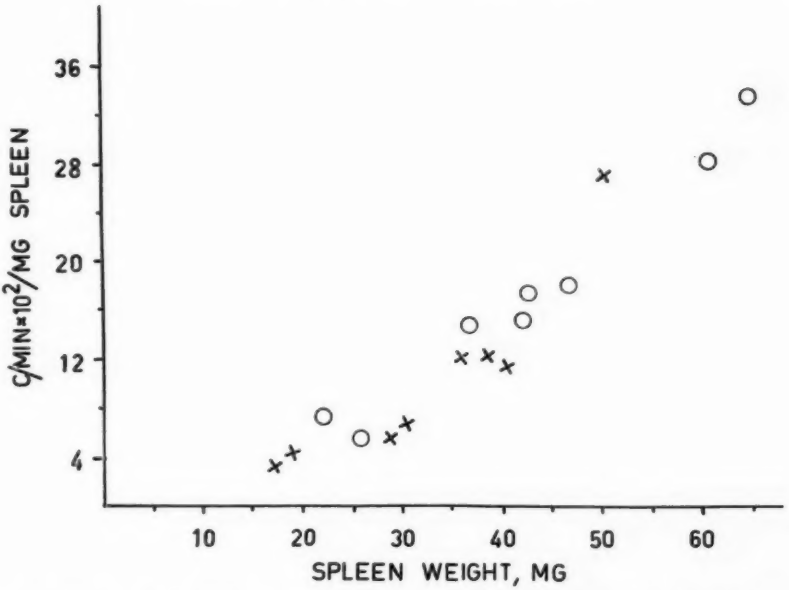
in the 'saline + 725 r' group but improves substantially during the second week. There also seems to be a net increase in the total amount of haemin as well as of the Fe^{59} activity of the haemin. In one experiment 0.27 μC Fe^{59} was given per animal on the 12th day after irradiation and the haemin isolated 24 hrs later (Table 4).

In further experiments the question arose as to whether the increase in spleen weight reflected a synthesis of new tissue substance, or was due

Table 4

Sampled blood from 12 animals in each group

Group	Mg haemin crystals per 5 ml blood sediment	Fe^{59} activity, c/min
PPP + 725 r + lycopene	4.14	1 980
Saline + 725 r + saline	2.94	688



The incorporation of C^{14}-2-glycine into proteins and nucleic acids of PPP + 725 r + 50 γ lycopene-treated mice (o), as compared to saline + 725 r + saline-treated mice (×). Male mice, weighing 27 g, were used in groups of thirty. Specific activities on the eighth day following irradiation has been plotted against weights of fresh spleens.

at least partly to phagocytic activity. The incorporation of C^{14}-2-glycine into the proteins and nucleic acids was therefore assayed during the recovery period. One group of animals was given 2 mg PPP, followed by 725 r after 24 hrs and 50 γ lycopene 30 min following the dose. In the other group saline was injected instead of PPP-lycopene. Four animals from each group had C^{14}-2-glycine on days 7 and 9, and were sacrificed and analysed 24 hrs later (See diagram above). The results imply that the specific activity increases with the weight of the spleens.

The incorporation of labeled glycine and thus the synthesis of proteins and nucleic acids at the time of analysis was consequently proceeding at a higher rate in spleens in which the recovery, as judged from the weight, had gone further. The corresponding Fe^{59} data (Table 3) do not show the same clear relationship between spleen weight and Fe^{59} specific activity. Thus the two processes of haemin- and protein-nucleic acid synthesis do not run parallel as even spleens of low weight can occasionally show a high synthetic rate of haemin and vice versa.

Discussion

In continuity of earlier work the mechanism of the lycopene action in stimulating recovery of irradiated mice was further investigated. The timing of the lycopene injection relative to the radiation is of prime importance, as was demonstrated in an earlier publication. We have attempted to control the initial steps of the lycopene action by pretreatment with polyphloretin phosphate. This supplementary treatment was found to be of some advantage and, although the mechanism of the PPP action was not obvious, it may be presumed that the substance acts in a moderating way on the resorption of lycopene.

The difficulty in exercising control over all the experimental variables has already been emphasized. The whole procedure may be worked out to fit a particular strain of animals of a certain physiologic age but needs modification if the animal material is altered.

It has been demonstrated by many workers that substances which are injected as particle suspensions stimulate the recovery of radiated animals. Since some of the compounds which have been used are not biologic in nature, e. g. ground glass and similar inorganic materials, a rather unspecific kind of stimulation of some inherent recovery functions is perhaps operating and it may well be that lycopene, although also a compound of biologic importance, acts in a similar manner.

The recovery in the chemically treated groups is accompanied by a more vigorous and perhaps also earlier stimulation of synthesis of new spleen tissue as well as of haemopoietic activity. This is however true only in regard to average figures, since some mice in the chemically untreated groups display similar or even higher Fe^{59} and C^{14} values than the average of treated mice (Table 3 and the diagram, p. 397). The synthetic rate of new spleen tissue, in particular, as may be seen from the diagram, seems to suggest that lycopene mainly gives an extra stimulus to recovery processes which are operating already in animals which have been irradiated without any additional chemical treatment.

Attempts to demonstrate a relationship between the early capacity of haemin synthesis and formation of new erythrocytes on the one side, with prospects for survival on the other, gave as already stated a rather weak correlation between the Fe^{59} activity of circulating erythrocytes and the chances for survival. The significance of this is that stimulation of haemopoiesis is only one factor in the recovery mechanism. Another group of workers has demonstrated a strong antibacterial effect of lycopene (10). Since bacteremia is recognized as part of the radiation syndrome, the lycopene action is certainly also due to this antibacterial property.

We have in addition found a weight increase of the suprarenals during

ıe recovery period. BACQ noted a weight increase of the suprarenals of ıts 2 to 4 days following irradiation with 800 r but not in animals given ıe protection of cysteamine before irradiation (1). On the other hand ıere was a drop in the ascorbic acid and cholesterol concentration in non-rotected animals but not in protected ones. In further work BACQ also emonstrated that radiation changes in the suprarenals was dependent n the anterior pituitary gland (2). Since we have no biochemical data in ur mice material, the weight increase in the lycopene treated groups is not asily understood or possible to discuss in relation to BACQ's data.

There is however evidence by ELLINGER that desoxycorticosterone njections reduce the mortality of irradiated rats (3). Similarly, LANGEN-ORFF et coll. (8, 9) found a slight protection in irradiated mice through lesoxycorticosterone as well as from 'suprarenal extract'. Implantation of suprarenal tissue after the irradiation seems to provoke an increased recovery. In view of this the participation of suprarenals and hormones is likely an additional part of the total recovery process, and the weight increase found in our material may indicate an increased hormonal activity.

Acknowledgements

This investigation was generously aided by grants from the Swedish Atomic Energy Committee, the Knut and Alice Wallenberg Foundation, and the Swedish Cancer Society.

SUMMARY

The action of lycopene administered after irradiation was investigated in a large series of mice. Some of the experiments showed that the results were improved by an initial dose of polyphloretin phosphate (PPP). A possible increase in suprarenal function in the treated animals was observed.

ZUSAMMENFASSUNG

Die Wirkung von Lykopen, das nach Röntgenbestrahlung verabreicht worden war, wurde an einer grossen Serie von Mäusen untersucht. Eine der Versuche zeigten, dass die Resultate durch initiale Gaben von Polyphloretinphosphat (PPP) verbessert werden konnten. Möglicherweise wurde auch eine Steigerung der Nebennierenfunktion der behandelten Tiere beobachtet.

RÉSUMÉ

Les auteurs ont expérimenté sur une importante série de souris l'action du lycophène administré après irradiation. Certaines de ces expériences ont montré que les résultats sont améliorés par une dose initiale de phosphate de polyphlorétine (PPP). Ils ont constaté sur les animaux traités une augmentation possible du fonctionnement surrénalien.

REFERENCES

1. BACQ, Z. M. and ALEXANDER, P.: Fundamentals of radiobiology. Butterworth London 1955.
2. — MARTINOVIC, P., FISCHER, P. et coll.: Adrenal changes after wholebody irradiation in the hypophysectomised rat grafted with pituitary tissue in the anterior chamber of the eye and of the adrenalectomised rat grafted with adrenal tissue in the eye. Advances in radiobiology. Oliver and Boyd, Edinburgh 1957.
3. ELLINGER, FR.: Influence of pharmacological agents on effects of irradiation. Radiology 50 (1948), 234.
4. FORSSBERG, A., LINGEN, CHR., ERNSTER, L., and LINDBERG, O.: Modification of the X-irradiation syndrome by lycopene. Exp. Cell. Res. 16 (1959), 7.
5. FRIES, B.: Polyphloretin phosphate — a hyaluronidase inhibitor — and hyaluronidase in prevention of intraperitoneal adhesions. Acta Chir. scand. Suppl. 217 (1956).
6. — and WALINDER, G.: Absorption of colloidal Au^{198} from peritoneum and pleura and its inhibition by polyphloretin phosphate. Acta radiol. 48 (1957), 113.
7. — KOTTMEIER, H. L. and WALINDER, G.: Treatment of peritoneal carcinosis with colloidal Au^{198} in combination with polyphloretin phosphate. Acta radiol. 52 (1959), 81.
8. LANGENDORFF, H., KOCH, R. und SAUER, H.: Der Einfluss des Desoxycorticosterons und Nebennierenrindenextrakten auf den Ablauf der tödlichen Röntgenbestrahlung. Strahlentherapie. 93 (1954), 37.
9. — — — Der Einfluss von Desoxycorticosteron-Kristallimplantaten und Nebennierenimplantationen auf die Überlebensrate röntgenbestrahlter Mäuse. Strahlentherapie. 93 (1954), 44.
10. LINGEN, G., ERNSTER, L. and LINDBERG, O.: The promoting effect of lycopene on the non-specific resistance of animals. Exp. Cell Res. 16 (1959), 384.

FROM THE PHYSICS DEPARTMENT (CHIEF PHYSICIST: L. A. W. KEMP), LONDON HOSPITAL, WHITECHAPEL, LONDON, ENGLAND

PHYSICAL ASPECTS OF COBALT 60 TELETHERAPY USING WEDGE FILTERS

I. Physical investigations

by

M. Cohen, J. E. Burns and *R. Sear*

One of the distinguishing features of roentgen therapy as practised at the London Hospital for many years past is the extensive use made of wedge filters (Ellis, Shanks, Oliver and Kemp 1950). Indeed, more recently the subject has been studied intensively and largely systematized (Cohen 1959, Cohen and Burns 1959). In view of the experience thus gained, it was decided to develop wedge filters for a Picker C 3000 cobalt 60 teletherapy unit when the unit was installed in 1956. These wedge filters were to serve, not as an auxiliary tool to be used only occasionally, but as an essential technique for regular and frequent use. This being the case, the production and application of these filters was approached, *ab initio*, in a more systematic fashion than has hitherto been described in the literature concerning Co^{60} teletherapy (Fletcher 1956, Tulley 1956; see also, for wedge filters designed for use with high-energy roentgen-ray generators, Day and Farmer 1958, François 1958 and Tranter 1957).

Construction of wedge filters. Although the mass absorption coefficient of cobalt γ-rays (1.17 and 1.32 MeV) is not very dependent on the atomic number of the absorbing material, lead was considered to be the most

Submitted for publication 14 September 1959.

Table 1

Dimensions in wedge direction of lead (0.5 mm thick throughout) used for construction of wedge filters

Wedge size	First step	Number of increments of size stated (p) and step dimension reached					Total number of steps	Aperture (i.e. beam) width
		p = 4 mm	p = 3.5 mm	p = 3 mm	p = 2.5 mm	p = 2 mm		
4 cm	3 mm	2 (11 mm)	1 (14.5 mm)	1 (17.5 mm)	3 (25 mm)	3 (31 mm)	11	34 mm
5 cm	7 mm	2 (15 mm)	1 (18.5 mm)	1 (21.5 mm)	3 (35 mm)	3 (35 mm)	11	42 mm
6 cm	8 mm	4 (24 mm)	2 (31 mm)	4 (43 mm)	—	—	11	49 mm
8 cm	8 mm	3 (20 mm)	2 (27 mm)	4 (39 mm)	6 (54 mm)	—	16	64 mm
10 cm	8 mm	2 (16 mm)	4 (30 mm)	4 (42 mm)	9 (64.5 mm)	—	20	79 mm

suitable material for the construction of wedge filters, since its high density permits a compact design which facilitates handling and (assuming that the wedge is placed at the end of the collimator) enables the distance between the wedge material and the skin to be maximal for a given unit. At the same time, fabrication of experimental wedge filters from thin lead sheets, during the design stage, is both simple and rapid.

The wedge of laminated lead is fixed to a thin aluminium plate and thence to a duralumin base-plate approximately 20 cm square and 6 mm thick. A suitable aperture is cut in the latter, to avoid the loss in beam intensity (about 9 %) which would otherwise result from absorption in the duralumin. Constructional details are given in Table 1 and in Fig. 1 (A and B). An important detail which cannot be shown in the diagram is that each step of the wedge is glued to its neighbours by an impact adhesive and the edges of the completed wedge are soldered before it is fixed to the aluminium mounting plate. These precautions are necessary to prevent distortion of the lead wedge during use. A photograph of one of the filters is given in Fig. 2. The wax compensating wedge also shown in the picture will be described in part II of this paper.

The filter base-plates are inserted in a special slide (see Fig. 1 — C) which is screwed permanently to the end of the collimator. The wedge itself is fixed to its base-plate in such a way that when inserted in the slide the thick side of the wedge corresponds to the open end of the slide. The reason for this will be explained in part II in the section on setting-up. When the wedge is in position in the slide it is approximately 16 cm from the skin assuming the latter is at the working SSD (80 cm). As a

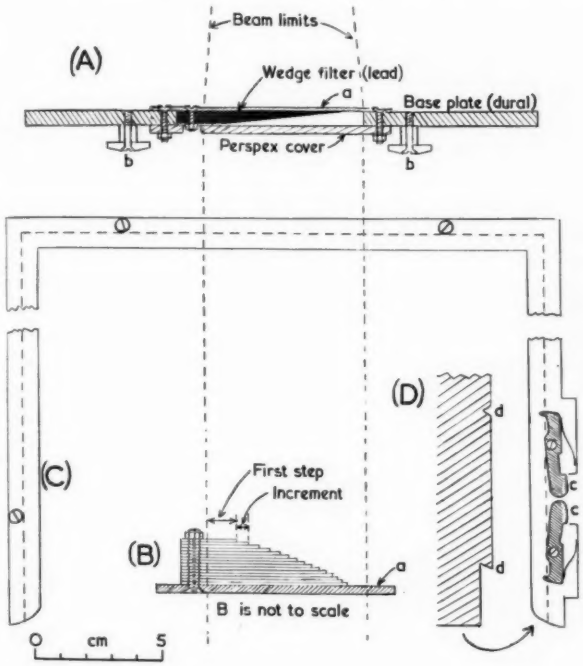


Fig. 1. Construction of wedge filter and slide.

A — Section through base plate and wedge;

B — Diagram of wedge (see Table 1);

C — Plan of filter slide;

D — Corner of base plate (plan);

a — Aluminium plate (1 mm) on which wedge is mounted;

b, b — Retaining brackets for holding the wax compensating wedge;

c, c — Spring-loaded safety catches which locate in d, d;

d, d — Notches cut in the base-plate.

safety measure the slide is fitted with two independent catches which locate in notches in one side of the base-plate, thus ensuring that the filter can be inserted only the correct way round (Fig. 1 — D). The two catches are adjacent so that they are released simultaneously by a single thumb action.

The Picker unit is provided with an optical simulator which gives a visual indication of the field dimensions on the patient, although at the same time the precise field dimensions may be set on the calibrated collimator knobs. The routine use of the simulator for setting-up wedge fields (see part II) renders unnecessary any mechanical interlock between the collimator and the wedge inserted.

Design of wedge filters. Throughout this paper the term 'field width' will be used to denote the field dimension in the wedge direction while 'field length' will refer solely to the non-wedge direction.

In designing wedge filters for a cobalt unit, advantage may be taken of the fact that cobalt γ-rays are scattered to only a small extent in an

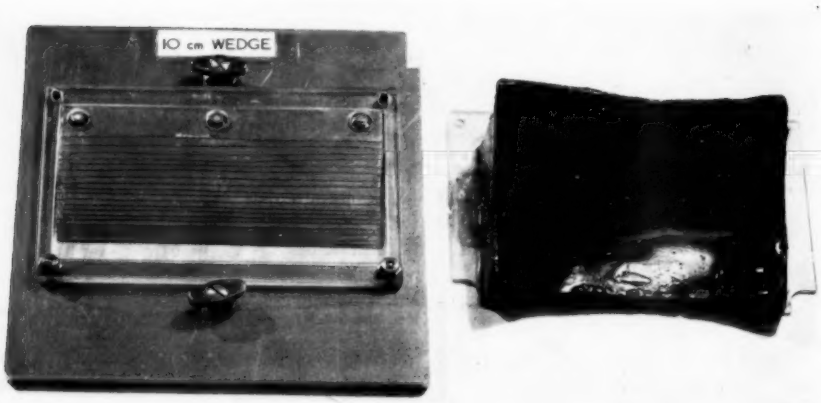


Fig. 2. Wedge filter and wax compensating wedge.

absorbing medium. As a working basis it was assumed that: (1) the dose at any point in tissue (and hence the dose distribution as a whole) depended only on the primary radiation reaching the point via known thicknesses of wedge filter and tissue and (2) the dose distribution for a given wedge was independent of the field length (i. e. in the non-wedge direction.)

Since scatter is not entirely absent these assumptions are approximate only, but in practice they served as a convenient starting point. Thus the initial design of each wedge was based essentially on an absorption curve of the radiation in lead measured with a narrow beam (defined by a 2.5 cm diameter aperture in a lead block) under conditions of 'good geometry'. Furthermore, the isodose curves of each wedge filter, when measured with different field lengths, were found to lie sufficiently close together to justify the production of a single wedge for each field width to serve over a wide range of field lengths. It will be shown that, except in the case of the 10 cm wedge, a single mean isodose chart suffices for each wedge, covering all field lengths to the accuracy required for clinical purposes.

The wedges chosen, in consultation with the radiotherapeutic staff, were as follows: 4 cm wedge for field length range 4 to 12 cm; 5 cm, 6 cm and 8 cm wedges for field length range 4 to 16 cm; 10 cm wedge for field length range 4 to 20 cm.

In order to allow for the fact that, for a given wedge the field length is continuously variable within the range stated, the following terminology

has been adopted: a wedge of field width m and field length n is denoted by $mW \times n$, the dimensions being in centimetres throughout. The minimum length of 4 cm is governed by the construction of the Johns-Mackay collimator. The dimensions given are those at the working SSD (80 cm); the actual dimensions of the wedges are, of course, proportionately decreased to allow for the divergence of the beam (see Table 1).

Physical investigations

Measurement of isodose curves. Isodose curves were measured in a water phantom, contained within a perspex tank about 40 cm cube, by means of an automatic isodose plotter built by the General Electric Company, Wembley, England, to a design originated by KEMP (1946). The exploring chamber was 6 mm in diameter and was fitted with a pure graphite cap. The chamber response was known to be independent of wavelength over the entire range likely to be encountered within the phantom.

For each wedge two or three trial isodose curves were plotted for each of three field lengths (short, medium and long), and corrections made to the wedge design as necessary. In most cases three such trials sufficed to establish a satisfactory wedge specification which yielded straight isodose lines of approximately 45° slope for the whole range of field lengths required. No attempt was made, however, to produce isodoses at precisely 45° and, in fact, in no case was the mean slope of the final isodose curves (as denoted by the 'wedge angle', Ø, to be defined in part II), exactly 45°.

The isodose curves of the final wedge specifications were plotted in full for each of three field lengths, i. e. the minimum (4 cm), the maximum (12, 16 or 20 cm according to the wedge) and an intermediate length (usually 8 cm). The presentation of the final isodose curves will be described below.

Build-up studies. It is of some importance to study the effect on build-up of interposing a wedge filter. In the work on non-wedge fields for the Picker cobalt unit reported by KEMP and BURNS (1958), build-up curves were measured by means of a β-ray chamber built into a large sheet of perspex which was placed on top of an enclosed water phantom. This chamber had an air volume 4 cm in diameter and 1 mm deep, while the diameter of the collecting electrode was 2 cm. It was felt, however, that this chamber was too large for work with wedge fields, in which the dose-rate varies quite rapidly laterally as well as axially. A smaller β-ray chamber was, however, available in which the collecting electrode was 1 cm in diameter and the air volume 1 mm deep $\times$ 1.7 cm diameter;

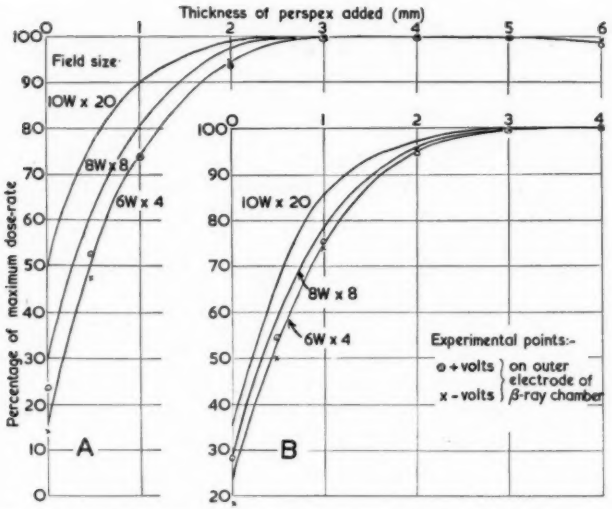


Fig. 3. Build-up curves for wedge fields. A — Central axis, B — At position of maximum surface dose (hot-spot).

the front wall was graphited cellophane (approx. 7 mg/cm^2). Considerations of sensitivity would not allow these dimensions to be further reduced, but it is considered that the error introduced by the chamber actually used was small in all situations except at the edge of the field.

The chamber was built into the upper surface of a solid phantom constructed of sheets of Mix D wax (JONES and RAINE 1949), together with 'Lincolnshire' bolus (LINDSAY and STERN 1953), contained in a wooden box. By means of a sensitive version of the ionization current comparator (KEMP 1945), recently described by KEMP and BANFIELD (1957), the ionization current was measured relative to a standard current obtained from a 'β-ray reference chamber' (KEMP and BURNS 1958) containing a source of β-radiation (S^{35}). (Although the use of a comparator technique is unnecessary with a cobalt unit from the point of view of eliminating the effects of fluctuations in radiation output, there are other important advantages in retaining this technique. e. g. the high intrinsic accuracy of a null method, the facility of a direct-reading scale which can be set to 100 as required, and the elimination of temperature-pressure effects.)

The build-up curves were measured by placing thin sheets of perspex over the front wall of the chamber. Each measurement was made twice, by reversing the polarity of the voltage applied to the chamber.

and averaging the two currents. The necessity for reversing the chamber voltage was pointed out by RICHARDSON (1954) and by KEMP and BARBER (1958). The phenomenon has recently been investigated in detail by JOHNS, ASPIN and BAKER (1958).

Build-up curves measured on the central axis for small, medium and large fields, are shown in Fig. 3 — A. In one case (6 W × 4), the experimental points are included to indicate the magnitude of the polarity effect just mentioned. The curves in Fig. 3 — B are for the same fields, but were measured at the position of the 'hot-spot', i. e. the position of maximum dose across the surface (see below).

By comparing Fig. 3 with the corresponding curves for non-wedge fields (KEMP and BURNS 1958), it is seen that the interposition of a wedge filter makes no important difference to the build-up characteristics of the radiation. With small fields the maximum occurs at about 4 mm of perspex (corresponding to approximately 5 mm of unit density material), but in all cases the curve is fairly flat between about 2 and 6 mm of perspex. There is no essential difference between the build-up on the central axis and at the position of the 'hot-spot'. This is important, since, in view of the limitations placed on wedge therapy at conventional qualities by the existence of a region of high skin dose (COHEN 1959), it is desirable to ensure that nothing is done during the actual treatment of patients to destroy the build-up characteristics of the cobalt radiation at the 'hot-spot'.

The comparison between wedge and non-wedge fields is illustrated in Fig. 4, in which the points refer to the percentage dose obtained at the surface for wedge fields, while the full curve has been plotted from data given for non-wedge fields by KEMP and BURNS (1958). In view of the difficulty in assessing the surface dose accurately, because the polarity effect is most marked in this position (giving rise to a spread of about ± 20 % in the experimental points; see Fig. 3), the virtual identity of wedge and non-wedge build-up characteristics is satisfactorily demonstrated.

Cross-beam variation and the 'hot-spot'. The build-up apparatus was also used for determining the cross-beam variation at the depth of maximum build-up, taken as 5 mm of water (i. e. 4 mm of perspex) throughout. The results for the 8 cm wedge are shown in Fig. 5, from which it is seen that the lateral situation of the 'hot-spot' is independent of the length of the field. In the case of the 8 cm wedge the 'hot-spot' occurs at 8 mm, i. e. 0.1 of the width of the wedge, from the field edge. This was found to be true also (to a close approximation) for all the other wedges, and also corresponds to the situation previously reported for wedges designed for 250 kV roentgen rays (COHEN and BURNS 1959).

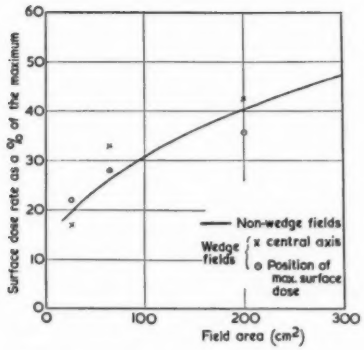

Surface dose rate as a % of the maximum
Field area (cm²)
Non-wedge fields
Wedge fields
x central axis
o Position of max. surface dose

Fig. 4. Comparison of percentage dose at the surface for wedge and non-wedge fields.

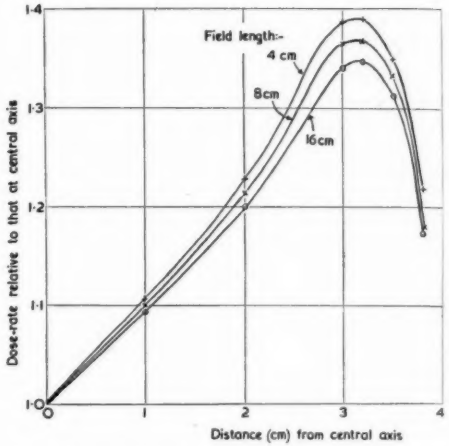


Fig. 5. Lateral distribution of dose at a depth of 5 mm (4 mm perspex), in the direction of the hot-spot, for an 8 cm wedge.

Having determined the position of the hot-spot, the dose at this point was measured and expressed as a percentage of the central axis dose. The resulting curves for a number of field lengths are given in Fig. 6. It is seen that, for a given wedge, the percentage dose at 5 mm depth at the hot-spot falls with increasing field length, but the effect is so small as to be practically insignificant in therapy. It is interesting to note that for a given wedge the hot-spot dose is much lower than for the corresponding copper wedge designed for 250 kV roentgen rays, although the isodose curves in the two cases are of comparable slope at medium depths (COHEN 1959). This difference may be explained by the low level of scattered radiation at cobalt qualities and also by the homogenous nature of the radiation so that no hardening of the beam occurs on the thick side of the wedge. The latter effect has been shown to result in an increased hot-spot dose for copper wedges used with deep roentgen rays (COHEN 1960).

Central axis percentage depth doses. In the range 0.5 to 5 cm depth these were measured with the build-up apparatus in conjunction with an overlying perspex tray containing water. From 2 to 25 cm depth a thimble chamber in a water phantom was used; thus the two types of measurement overlapped in the range 2 to 5 cm.

These data were used for correcting the positions of the isodose curves previously measured, since for practical reasons the latter could

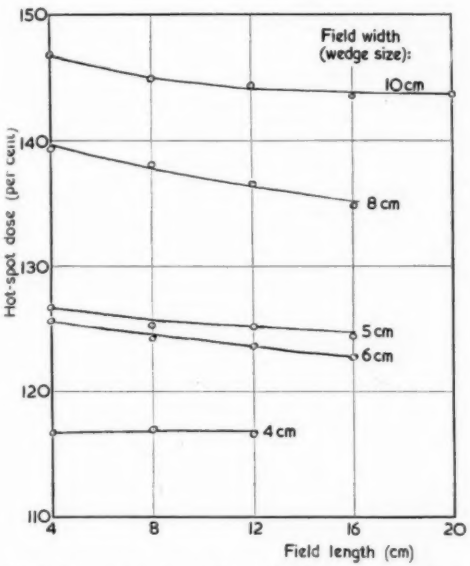


Fig 6. Percentage dose at 5 mm depth at position of hot-spot. Anomalous position of the 6 cm wedge curve due to fact that this wedge is somewhat less steep than the other wedges. (Cf. Table 1, part II.)

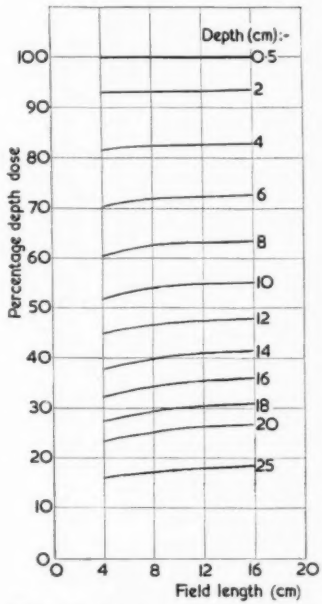


Fig 7. Variation of percentage depth dose with field length (5 cm wedge).

not be plotted relative to the true '100 %' point. Furthermore, the central axis data enabled mean isodose curves (independent of field length) to be fixed for each wedge. This was done by plotting percentage depth dose against field length for each wedge, an example (for the 5 cm wedge) being given in Fig. 7. It was found that, if depths from 6 to 15 cm only were considered (corresponding to the tumour depth in the majority of two-field arrangements), a mean field length could be found such that the variation in percentage depth-dose at any given depth did not exceed $\pm$ 5 % over the whole range of field lengths used. The numerical value of the mean field length was somewhat greater for large wedges than for small, but it was felt that for clinical purposes it was more important to select a single length for use with every wedge than to insist on the highest degree of accuracy. The most appropriate length for this purpose appeared to be 7 cm, but as it was not considered desirable to present 'mean' isodose curves with this odd value of field length, 6 cm was used instead. In the case of the 10 cm wedge, a second mean length of 12 cm was required (covering the range 8 to 20 cm) in order to preserve approximately the limits of $\pm$ 5 %.

Two examples of the isodose curves in use at the London Hospital

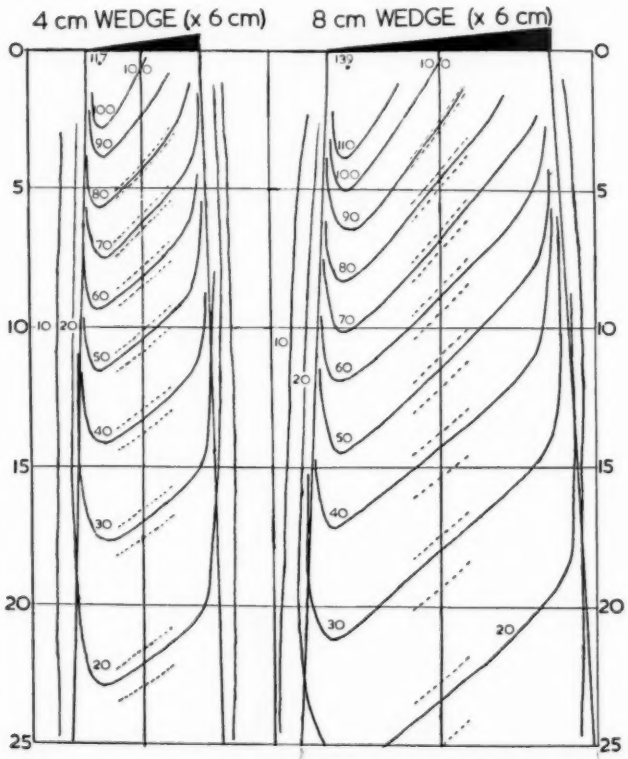


Fig 8. Isodose curves of wedge fields. Full lines are for field length 6 cm, upper broken lines for 4 cm, lower broken lines for field lengths of 12 cm in case of 4 cm wedge, and 16 cm in 8 cm wedge.

are shown in Fig. 8. The curves for the other wedges are similar. In practice it has not been necessary for the radiotherapeutic staff to make extensive use of these charts, since full data have also been provided for a complete range of two-field treatment arrays as will be described in part II.

Field factors. When the unit was installed, the 'standard output', i. e. exposure dose-rate in r/min, was measured in air at 80 cm from the source, using a 4×4 cm field. The output value has since been adjusted at intervals to allow for the decay of the source. For clinical purposes the absorbed dose-rate, in rads/min at the '100 %' point for any given field, is obtained by multiplying the prevailing 'standard output' by a factor which KEMP and BURNS (1958) called the 'overall field factor'.

Table 2

Field factors for wedge fields

Field length (cm)	Field width (cm) 4	5	6	8	10
4	0.703	0.714	0.704	0.660	0.639
5	0.707	0.719	0.710	0.666	0.646
6	0.710	0.724	0.715	0.672	0.652
7	0.713	0.728	0.719	0.678	0.657
8	0.716	0.732	0.723	0.683	0.662
9	0.719	0.735	0.727	0.687	0.667
10	0.721	0.738	0.730	0.691	0.671
11	0.723	0.741	0.733	0.695	0.675
12	0.725	0.744	0.735	0.698	0.679
13		0.747	0.737	0.701	0.683
14		0.749	0.739	0.704	0.686
15		0.751	0.741	0.706	0.689
16		0.752	0.742	0.708	0.692
17					0.694
18					0.696
19					0.698
20					0.700

The field factors measured for wedge fields are set out in Table 2, from which it is seen that their values range from 0.64 to 0.75, the factor decreasing with field width and increasing with field length. This means that, with a source of 1 500 curies the dose-rate at the '100 %' point is about 30 rads/min, and the exposure time for a typical 2-field treatment session, giving 200 rads tumour dose (percentage depth dose ~ 130 %), is about 5 min for each field.

The values given in Table 2 serve as a guide to the relative magnitude of the field factors for different wedges and field lengths. It is advisable, however, to check the factor for any newly-constructed wedge. This may be done by measuring the dose-rate at any convenient point in a phantom at which the percentage depth dose is known, the r/rad conversion factor being taken as 0.975 in water for cobalt 60 γ-rays.

Copies of the isodose charts for single wedge fields may be obtained through the Diagrams and Data Scheme of the Hospital Physicists' Association. (Hon. Secretary: Mr. C. Gregory, Mount Vernon Hospital, Northwood, Middlesex, England.)

SUMMARY

Wedge filters for use with a Picker C 3 000 cobalt unit are described. Measurements were made of build-up, transverse field distributions, percentage depth doses, isodose curves and absolute dose-rates. It is shown that the presence of a wedge filter does not

appreciably alter the build-up characteristics of the radiation. For a given wedge (i. e. a given field width) a single isodose chart suffices for all field lengths, within limits of ± 5 %.

ZUSAMMENFASSUNG

Keilfilter für eine Picker C 3 000 Kobaltapparatur werden beschrieben. Messungen über Aufbau, transversale Feldverteilung, prozentuelle Tiefendosis, Isodosenkurven und absolute Strahlendosen wurden ausgeführt. Es wird gezeigt, dass das Keilfilter die Eigenschaften des Dosis-Aufbaus der Strahlung nicht wesentlich verändert. Für einen bestimmten Keil genügt eine einfache Isodosentabelle für sämtliche Feldlängen innerhalb einer Grenze von ± 5 %.

RÉSUMÉ

Les auteurs décrivent des filtres en coin utilisables avec un appareil de cobaltthérapie Picker C 3 000. Ils ont mesuré le 'build-up' de dose, la distribution transversale dans les champs, les pourcentages de dose en profondeur, les courbes isodoses et les débits de dose absolus. Ils montrent que la présence d'un filtre en coin ne modifie pas appréciablement les caractéristiques du 'build-up' de rayonnement. Pour un filtre donné, (c'est-à-dire pour une largeur de champ donnée), une seule table d'isodoses suffit pour toutes les longueurs de champs, dans une limite de ± 5 %.

REFERENCES

COHEN, M.: Physical aspects of roentgen therapy using wedge filters. I. Some new copper wedges and their applications. II. Analysis of wedge field dosimetry. Acta radiol. 52 (1959), 65, 158. IV. A new wedge principle using graphite and tin. Acta radiol. 53 (1960), 153.

— and BURNS, J. E.: Physical aspects of roentgen therapy using wedge filters. III. The effect on wedge fields of variations in kV and other factors. Acta radiol. 52 (1959), 470.

DAY, M. J. and FARMER, F. T.: The 4 MeV linear accelerator at Newcastle upon Tyne. Brit. J. Radiol. 31 (1958), 669.

ELLIS, F., SHANKS, W., OLIVER, R. and KEMP, L. A. W.: The use of wedge filters in X-ray therapy. J. Fac. Radiol. 1 (1950), 231.

FLETCHER, G. H.: Clinical stationary field therapy with a cobalt-60 unit. Amer. J. Roentgenol. 75 (1956), 91, 117.

FRANÇOIS, P. E.: Wedge filters for use on the 8 MeV linear accelerator. Brit. J. Radiol. 31 (1958), 712.

JOHNS, H. E., ASPIN, N. and BAKER, R. G.: Current induced in the dielectric of ionization chambers through the action of high energy radiation. Rad. Res. 9 (1958), 573.

JONES, D. E. A. and RAINE, H. C.: Mix D (Letter). Brit. J. Radiol. 22 (1949), 549.

KEMP, L. A. W.: A new circuit with special applications in gamma-ray and X-ray dosimetry. Brit. J. Radiol. 18 (1945), 107.

— The exploration of X-ray dose distribution: an automatic method. Brit. J. Radiol. 19 (1946), 488.

– and BANFIELD, B. J.: A portable ionization current comparator. J. Sci. Instrum. 34 (1957), 27.
– and BARBER, B.: The basic design of a guarded-field thimble ionization chamber: a precision ionometric investigation. Phys. Med. Biol. 3 (1958), 123.
– and BURNS, J. E.: Physical measurements on the London Hospital Picker C 3 000 cobalt unit. Acta radiol. 49 (1958), 471.
LINDSAY, D. D. and STERN, B. E.: A new tissue-like material for use in radiotherapy. Radiology 60 (1953), 355.
RICHARDSON, J. E.: Effect of chamber voltage on electron build-up measurements. Radiology 62 (1954), 584.
TRANTER, F. W.: Design of wedge filters for use with a 4 MeV linear accelerator. Brit. J. Radiol. 30 (1957), 329.
TULLEY, T. J.: Wedge filters for use with a 100-curie cobalt-60 teletherapy unit. Brit. J. Radiol. 29 (1956), 227.

BOOKS RECEIVED

We acknowledge with thanks under this heading books received for review, which we trust will be regarded as a sufficient mark of appreciation of the courtesy of the sender. The reviews of selected items will appear as soon as opportunity affords.

LA CARTOGRAPHIE THYROÏDIENNE. Méthode cartographique et applications cliniques. Par Jean Martin. Société d'Impressions Typographiques, Nancy 1958.

MALIGNANT DISEASE. UNIVERSITY COLLEGE HOSPITAL 1946—1950. Wilding & Son, Shrewsbury 1959.

LA STRATIGRAFIA DEI BRONCHI. Delle L. Oliva, R. Vignolini e G. L. Besio. La Minerva Medica, Torino 1959.

INTRACRANIAL CALCIFICATION. By Fermo Mascherpa and Vincenzo Valentino. Charles C. Thomas, Springfield, Ill., 1959.

MEDICAL RADIOGRAPHIC TECHNIC. Second Edition. Edited by Glenn W. Files. Charles C. Thomas, Springfield, Ill., 1959.

AN ATLAS OF NORMAL RADIOGRAPHIC ANATOMY. Second Edition. By Isadore Meschan. W. B. Saunders, Philadelphia and London 1959.

DAS DREHGLEITEN. Ein Teilproblem der Bandscheibendegeneration. Röntgenologie. Klinik und chiropraktische Aspekte. Von K. Reinhardt. — ÜBERBLICK ÜBER DIE FORTSCHRITTE AUF DEM GEBIET DER RÖNTGENOLOGISCHEN ABDOMINALDIAGNOSTIK. Von J. Hintze. Bibliotheca Radiologica Fasc. 1. S. Karger, Basel 1959.

DAS RÖNTGENSCHICHTBILD DES OHRES. Von K. Mündnich und K.-W. Frey. Georg Thieme, Stuttgart 1959.

RÖNTGENDIAGNOSTIK BEIM NEUGEBORENEN UND SÄUGLING. Von Hermann G. Wolf. Wilhelm Maudrich, Wien 1959.

MEDICAL X-RAY TECHNIQUE. By G. J. Van der Plaats. Philips' Technical Library, Eindhoven 1959.

DIE BEWEGUNGSBESTRAHLUNG. 2. völlig neubearbeitete Auflage. Von F. Wachsmann und G. Barth. Georg Thieme, Stuttgart 1959.

KLINIK UND PRAXIS DER UROLOGIE. KLINIK, INDIKATION, DIAGNOSTIK, OPERATIVE UND INSTRUMENTELLE EINGRIFFE, NACHBEHANDLUNG. Band I und II. Von W. Staehler. Georg Thieme, Stuttgart 1959.

RÖNTGENANATOMIE. Von W. Frik und U. Goering. Georg Thieme, Stuttgart 1959.

DAS DIAGNOSTISCHE PNEUMOPERITONEUM. Von A. Gebauer. Georg Thieme, Stuttgart 1959.

EINFÜHRUNG IN DIE RÖNTGENDIAGNOSTIK. Von U. Cocchi und P. Thurn. Georg Thieme, Stuttgart 1959.

DIE STREIFENATELEKTASEN DER LUNGE. Von Friedrich Heuck. Georg Thieme, Stuttgart 1959.

DIE PHLEBOGRAPHIE DER UNTEREN EXTREMITÄT. Von R. May und R. Nissl. Georg Thieme, Stuttgart 1959.

STRAHLENBELASTUNG UND STRAHLENSCHUTZ IN DER PÄDIATRISCHEN RÖNTGENDIAGNOSTIK. Von K. Hartung. Georg Thieme, Stuttgart 1959.

DAS RÖNTGENSCHICHTBILD. Von A. Gebauer, E. Muntean, E. Stutz und H. Vieten. Georg Thieme, Stuttgart 1959.

KLINISCHE RÖNTGENDIAGNOSTIK CHIRURGISCHER ERKRANKUNGEN. Von Hans Oberdalhoff, Heinz Vieten und Hermann Karcher. Springer Verlag, Berlin, Göttingen, Heidelberg 1959.

DIAGNOSIS OF CONGENITAL HEART DISEASE. 2nd ed. By Sven R. Kjellberg, Edgar Mannheimer, Ulf Rudhe and Bengt Jonsson. The Year Book Publishers, Chicago 1959.

CONTEMPORARY EQUIPMENT FOR WORK WITH RADIOACTIVE ISOTOPES. Consultants Bureau, New York 1959.

DETAILERKENNBARKEIT UND DOSIS BEI DER RÖNTGENDURCHLEUCHTUNG. Durchleuchtungsschirme und Bildverstärker. Von W. Frik. Alfred Hüthig Verlag, Heidelberg 1959.

ECHZIG JAHRE MEDIZINISCHE RADIOLOGIE. Probleme und Empirie. Von H. R. Schinz. Georg Thieme, Stuttgart 1959.

ELEKTROKYMOGRAPHIE. Von Karl Heckmann. Springer Verlag, Berlin, Göttingen, Heidelberg 1959.

ROENTGENS, RADS AND RIDDLES. A Symposium on supervoltage radiation therapy held at the Medical Division, Oak Ridge Institute of Nuclear Studies, July 15—18, 1956. United States Atomic Energy Commission, Washington 1959.

STRAHLENTHERAPIE VON HAUTKRANKHEITEN. Herausgegeben von A. Marchionini und C. G. Schirren. Springer Verlag, Berlin, Göttingen, Heidelberg 1959.

WILHELM CONRAD RÖNTGEN UND DIE GESCHICHTE DER RÖNTGENSTRAHLEN. 2. Auflage. Von Otto Glasser. Springer Verlag, Berlin, Göttingen, Heidelberg 1959.

CRÂNE ET FACE DANS LA MALADIE DE PAGET. Par J. A. Lièvre et H. Fischgold. Masson et Cie., Paris 1959.

DIAGNOSTIC RADIOISOTOPES. By Charles A. Owen Jr. Charles C. Thomas, Springfield, Ill., 1959.

LA FLEBOGRAFIA VERTEBRALE TRANSOMATICA. Delle G. Marcozzi, S. Messinetti, L. Saracca e M. Colombati. Edizioni Mediche e Scientifiche, Roma 1959.

HANDBUCH DER HAUT- UND GESCHLECHTSKRANKHEITEN. Band V/2: Strahlentherapie von Hautkrankheiten. Herausgegeben von A. Marchionini und C. G. Schirren. Springer Verlag, Berlin 1959.

RÖNTGENANATOMIE. Von D. Nagy. Verlag der ungarischen Akademie der Wissenschaften, Budapest 1959.

HEALTH PHYSICS INSTRUMENTATION. By John S. Handloser. Pergamon Press, London 1959.

STRAHLENBIOLOGIE, STRAHLENTHERAPIE, NUKLEARMEDIZIN UND KREBSFORSCHUNG. Herausgegeben von H. R. Schinz, H. Holthusen, H. Langendorff, B. Rajewsky und G. Schubert. Georg Thieme, Stuttgart 1959.

RADIOLOGIC EXAMINATION OF THE SMALL INTESTINE. Second edition. By Ross Golden. Charles C. Thomas, Springfield, Ill., 1959.

RADIATION BIOLOGY. Proceedings of the Second Australasian Conference on Radiation Biology held at the University, Melbourne 15—18 December 1958. Editor: J. H. Martin. Butterworth Scientific Publications, London 1959.

THE TREATMENT OF BRONCHIAL NEOPLASMS. By Robert E. Shaw and Donald L. Paulson. With a chapter on Bronchial adenoma by John Lester Kee Jr. Charles C. Thomas, Springfield, Ill., 1959.

AN ATLAS OF DENTAL AND ORAL RADIOLOGY. By Sydney Blackman. John Wright & Sons, Bristol 1959.

CINEFLUOROGRAPHY. Proceedings of the First Annual Symposium on Cinefluorography, Rochester November 14—15, 1958. Charles C. Thomas, Springfield, Ill., 1959.

SELECTED PAPERS FROM THE INSTITUTE OF CANCER RESEARCH: ROYAL CANCER HOSPITAL AND FROM THE ROYAL MARSDEN HOSPITAL. Vol. 12. The Chester Beatty Research Institute, London 1959.

TRANSVERSALE TOMOGRAPHIE. Experimentelle Untersuchungen zu den physikalisch-technischen Grundlagen der transversalen Tomographie und die klinischen Anwendungsmöglichkeiten. Von Franz Hammer. Wilhelm Maudrich, Wien 1959.

MEDICAL RADIOISOTOPE SCANNING. A seminar jointly organized by IAEA and WHO. International Atomic Energy Agency, Vienna 1959.

BOOK REVIEW

L'Encéphalographie fractionnée. Par Giovanni Ruggiero. 481 pages, 288 figures. Masson, Paris 1957.

The author was trained at Serafimerlasarettet, Stockholm, before his appointment as neuroradiologist at l'Hôpital Sainte-Anne, Paris in 1952. In close cooperation with the neurosurgical department, he has used and further widened his experiences by a systematic and critical revision of his material. He has long been an enthusiastic apostle of the encephalographic technique worked out at Serafimerlasarettet (encéphalographie fractionnée) and the results of his experience, as recorded in this monograph, are imposing. He presents his material meticulously and gives a detailed description of the technique, the normal anatomy of the cerebrospinal pathway, and the changes caused by various conditions, especially space-occupying lesions. Consideration is given to the hazards and value of the method, especially as compared with the other pneumographic methods of ventriculography and 'encéphalographie totale'. He claims in a convincing way that fractionnated encephalography in the hands of an experienced neuroradiologist is no more risky than ventriculography and in many cases is even better tolerated; it is considerably more informative. After analyzing the complications he concludes that they are in most cases probably caused by increased oedema rather than by coning, the latter often being demonstrable in the films. From the diagnostic point of view fractionnated encephalographie is in most cases superior to ventriculography, especially as it provides better chances of differentiating between extra- and intracerebral tumours.

The author has taken great pains to clarify the text by the inclusion of excellent illustrations. Each routine projection is illustrated by a photograph of the positioning as well as a reproduction of the corresponding film. The many photographs of cut slices of the brain to a great extent facilitate an appreciation of the rather complicated anatomy, especially that of the subarachnoid cisterns.

In the introduction the author writes: 'Tout au long de ce travail, je me suis inspiré d'une règle directrice: essayer de prouver ce que je disais'. This explains why the text in places sometimes makes rather heavy reading. Although unable to accept some of the statements made and the conclusions drawn, the reviewer regards this book as a most valuable contribution to our literature on modern encephalography — to his knowledge, the first more complete one in the French language.

Ingmar Wickbom